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Synthesis and Acid-Catalyzed Polymerization of 1,6-Anhydro-β-D-Glucopyranose Derivatives

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SYNTHESIS AND ACID-CATALYZED POLYMERIZATION OF 1,6-ANHYDRO-β-D-GLUCOPYRANOSE DERIVATIVES

A thesis submitted by

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SUMMARY

A number of 1,6-anhydrohexopyranoses were polymerized in the melt at 115° with the protic catalyst, monochloroacetic acid, under the conditions described by J. S. Carvalho, W. Prins, and C. Schuerch (7). The disappearance of a monomer was observed by trimethylsilylation of a reaction mixture followed by determination of the trimethylsilyl ether of a monomer by gas-liquid chromatography. In the early stages of polymerization (up to 40-50% monomer consumed), each monomer was found to disappear by a first-order rate process. The 1,6-anhydrohexopyranoses investigated and their relative rates of polymerization were: 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II) (1.0), 1,6-anhydro-3,4-di-O-methyl-β-D-glucopyranose (VII) (1.4), 1,6-anhydro-2-O-methyl-β-D-galactopyranose (XIII) (2.3), 1,6-anhydro-3-O-methyl-β-D-glucopyranose (III) (2.6), 1,6-anhydro-4-O-methyl-β-D-glucopyranose (IV) (6.3), 1,6-anhydro-4-O-(β-D-glucopyranosyl)-β-D-glucopyranose (XI) (9.0), 1,6-anhydro-β-D-galactopyranose (XII) (17), 1,6-anhydro-β-D-glucopyranose (I) (37), 1,6-anhydro-β-D-mannopyranose (IX) (91), and 1,6-anhydro-2-deoxy-β-D-arabino-hexopyranose (X) (240).

Monomers were consumed through polymerization as evidenced by paper, thin-layer, and gas-liquid chromatography. A 2-O-methyl-D-glucan with $\overline{Mn}$ of 1,030 and $[\alpha]_D^{25}$ +79.6° (water) was isolated after 16 days in 37% yield from the melt polymerization of 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II). Acid hydrolysis of the 2-O-methyl-D-glucan gave 2-O-methyl-D-glucopyranose which was identified by paper chromatography. Polymerization of 1,6-anhydro-2-deoxy-β-D-arabino-hexopyranose (X) for 4 hr. gave a 58% yield of synthetic polysaccharide which on hydrolysis followed by acetylation of the hydrolyzate gave crystalline 1,3,4,6-tetra-O-acetyl-2-deoxy-α-D-arabino-hexopyranose.

Replacement of any of the hydroxyl groups in 1,6-anhydro-β-D-glucopyranose (I) by a methoxyl group or replacement of the 4-hydroxyl group with a glucopyranosyl

group is seen to decrease the rate of disappearance of the 1,6-anhydro sugar, whereas replacement with a hydrogen atom for a hydroxyl group at the C-2 atom causes an acceleration of the polymerization rate. The effect of substitution on the rate of polymerization suggests this reaction is mechanistically related to the acid-hydrolysis of pyranosides. These data do not support the postulate of J. S. Carvalho, W. Prins, and C. Schuerch (7), and A. Bhattacharya and C. Schuerch, J. Org. Chem. 27:1895(1962), which states that some "intermediate related structurally to 1,2-anhydroglucopyranose" is necessary for polymerization to occur.

Two of the three possible monomethyl ethers and the 2,4-dimethyl ether of 1,6-anhydro-β-D-glucopyranose (I) were prepared for the first time. 1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II) was prepared by two independent routes. Pyrolysis of 2-O-methylcellulose (IIa) gave a 54% yield of the crystalline 2-methyl ether after purification through its dibenzoate. The formation of 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II) by pyrolysis supports the view of F. J. Kilzer and A. Broido (103) that cellulose degrades thermally through a 1,4-anhydro intermediate. 1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II) was prepared by the second route in an overall yield of 20% starting with 1,6-anhydro-β-D-glucopyranose (I). Using established procedures, 1,6-anhydro-β-D-glucopyranose (I) was converted to 1,6:3,4-dianhydro-2-O-methyl-β-D-galactopyranose (IIg) which, upon refluxing in aqueous potassium hydroxide, gave the desired product. Direct methylation of 1,6-anhydro-β-D-glucopyranose (I) under conditions favoring the yield of monomethyl ethers gave almost equimolar amounts of the 2- and 4-methyl ethers with also a trace of the 3-methyl ether. The composition of the mixture of ethers was analyzed by nuclear magnetic resonance spectroscopy.

1,6-Anhydro-4-O-methyl-β-D-glucopyranose (IV) was prepared by refluxing phenyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranoside (IVa) in aqueous alkali. This

phenyl glucoside was obtained in quantity by the modified Kuhn methylation of phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (IVc). Its characterization included an independent synthesis starting with the known 1,2,3,6-tetra-O-acetyl-4-O-methyl-β-D-glucopyranose (IVe).

1,6-Anhydro-2,4-di-O-methyl-β-D-glucopyranose (VI) was synthesized as a sirup by methylation of known 1,6-anhydro-3-O-acetyl-β-D-glucopyranose (VIa) with a mixture of diazomethane and boron trifluoride etherate followed by deesterification of the acetate in the usual manner with sodium methoxide in methanol.

Nuclear magnetic resonance (60 MHz) spectra of the seven methylated derivatives of 1,6-anhydro-β-D-glucopyranose (I) were measured in methyl sulfoxide-d_6 and deuterium oxide. Assignments of proton resonances for the pyranose ring were based on the splitting patterns of a proton signal and/or on spin-decoupling experiments. It was found that replacing a hydroxyl group with a methoxyl group shifts the proton resonance of the attached methine proton upfield while the proton signal of a methine proton on an adjacent carbon atom is moved slightly downfield. Empirical rules were formulated to correlate the chemical shifts of ring protons with the pattern of substitution of the methoxyl group using the chemical shifts of 1,6-anhydro-β-D-glucopyranose (I) as reference signals. The rules derived from the methyl ethers of 1,6-anhydro-β-D-glucopyranose (I) were also useful in predicting the chemical shifts of several protons in 1,6-anhydro-2-O-methyl-β-D-galactopyranose (XIII) and 1,6-anhydro-4-O-methyl-β-D-mannopyranose (XIV).

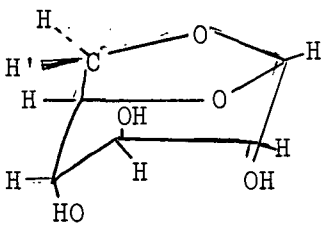
INTRODUCTION

The chemical synthesis of polysaccharides is of considerable interest, and has been reviewed most recently by Goldstein and Hullar (1). These authors have summarized the principal reasons for interest in this field:

> First, the present concepts of the chemical constitution of such important biopolymers as cellulose, amylose, and chitin can be confirmed by their adequate chemical synthesis. Second, synthetic polysaccharides of defined structure can be used to study the action pattern of enzymes, the induction and reaction of antibodies, and the effect of structure on biological activity in the interaction of proteins, nucleic acids, and lipides with polyhydroxylic macromolecules. Third, it is anticipated that synthetic polysaccharides of known structure and molecular size will provide ideal systems for the correlation of chemical and physical properties with chemical constitution and macromolecular conformation. Finally, synthetic polysaccharides and their derivatives should furnish a large variety of potentially useful materials whose properties can be widely varied; these substances may find new applications in biology, medicine, and industry.

A simple procedure which may be used to prepare a synthetic polysaccharide involves heating certain 1,6-anhydro aldoses in the melt and in the presence of an acid catalyst (1). Examples for the use of such synthetic polysaccharides may be found in References (1-3).

The first account of the preparation of a synthetic polysaccharide from a 1,6-anhydride occurred in 1918 when Pictet (4) heated 1,6-anhydro-β-D-glucopyranose (I)* at 240° to form a brown, viscous sirup. The addition of ethanol to this sirup precipitated polymeric material which, on the basis of its molecular weight (677,



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*See glossary of compounds, p. 47.

cryoscopy), Pictet concluded was tetramer. Platinum black (4, 5) and anhydrous zinc chloride (6) subsequently were observed to catalyze the polymerization of (I).

For nearly forty years little work was performed on the polymerization of 1,6-anhydro-β-D-glucopyranose (I). Then beginning in 1959 Schuerch, et al. (7, 8) reinvestigated the polymerization of (I) and a number of its tri-O-substituted derivatives. Polymerizations were performed in the presence or absence of either methyl sulfoxide or tetramethylene sulfone and with the addition of one of several protic acids — formic, acetic, monochloroacetic, phosphoric, or hydrochloric. The optimum conditions for polymerization of (I), which gave an amber-colored glass, occurred in the melt at 115-120° using monochloroacetic acid as catalyst in a mole ratio of monomer to catalyst of 50 to 1. 1,6-Anhydro-β-D-galactopyranose (XII) also polymerized using these conditions (9).

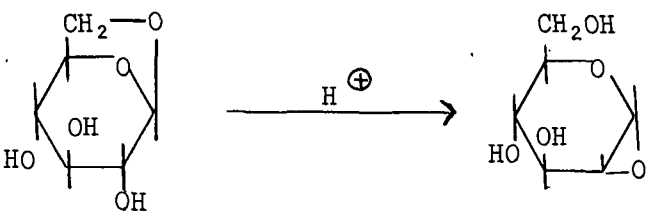
The synthetic glucan and galactan were precipitated with 85% ethanol. Yield of the glucan after heating (I) for 20 hr. at 116° was 66%, while the yield of galactan after 15 hr. heating at the same temperature was 76%. The weight average molecular weight, $\overline{M}_w$, of the glucan was initially reported to be 309,000 as determined by light scattering; the value was later corrected to 21,000 as found by ultracentrifuge. This abnormally high weight average molecular weight was attributed to the presence of "microgel" (10). The galactan had a number average molecular weight, $\overline{M}_n$, 1,800 and $\overline{M}_w$ 22,500 as measured by vapor-phase osmometry and ultracentrifugation, respectively. The great difference between $\overline{M}_w$ and $\overline{M}_n$ shows a marked polydispersity (1) in contrast to the relatively low polydispersity found in the naturally occurring polysaccharides, arabinogalactan and gum arabic (11, 12).

The specific optical rotations, $[\alpha]_D$, of the glucan (7) and galactan (9) in water were +91° and +82°, respectively. Assuming only that pyranoid units were present, the results of periodate oxidation of the glucan (7) correspond to 55% of

(1→6)-linkages, 35% of (1→4)- or (1→2)-linkages, and 10% of (1→3)-linkages [or (1→2)- and (1→4)-linkages]. Periodate oxidation studies on the galactan (9) revealed 43% of (1→6)-linkages, 56% of (1→4)- or (1→2)-linkages, and 1% of (1→3)-linkages [or (1→2)- and (1→4)-linkages].

1,6-Anhydro-β-D-mannopyranose (IX) has reportedly been polymerized (1, 13) to give a mannan in 25% yield under conditions identical to those used for the polymerization of (I).

In their work, Schuerch and coworkers attempted to elucidate the mechanism by which 1,6-anhydrohexopyranoses yield polymer under protic acid conditions. They observed that 1,6-anhydro-2-O-methyl-β-D-galactopyranose (XIII) was very resistant to polymerization (9) using the polymerizing conditions identical to those used on (I) and on 1,6-anhydro-β-D-galactopyranose (XII). Similarly, trisubstituted derivatives of (I), such as the trinitrate, the trimethanesulfonate, the tri-p-toluenesulfonate, the trimethyl ether (VIII), and the triacetate (Ib) failed to polymerize using several catalysts (8). The unreactivity of these trisubstituted derivatives of 1,6-anhydro-β-D-glucopyranose (I) and the 2-methyl ether of 1,6-anhydro-β-D-galactopyranose (XII) led Schuerch and coworkers to postulate (7, 9) that "some intermediate related structurally to 1,2-anhydroglucopyranose" was necessary for polymerization to occur. It was further postulated that the reactive 1,2-anhydride intermediate of α-D-glucopyranose then reacts with a free hydroxyl group to form a



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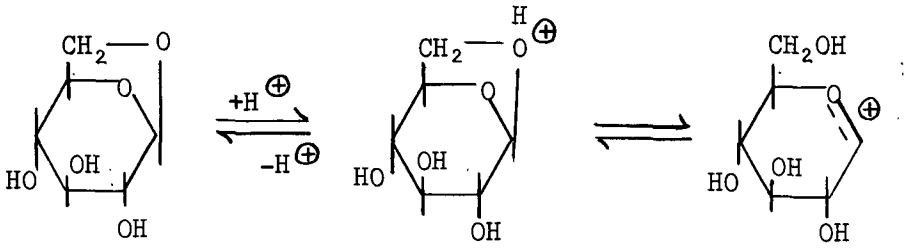
relatively stable glycosidic bond. Blocking of the 2-hydroxyl group prevents 1,2-anhydro formation and polymerization.

Another polymerization mechanism was postulated by Goldstein and Hullar (1), which is similar to the acid hydrolysis of glycosides (14). In a rapid equilibrium reaction, the oxygen atom of the 1,6-anhydride bridge is protonated. Ring-opening of the protonated molecule*, which is aided by a free 2-hydroxyl group in an undefined manner, gives a carbonium-oxonium ion that can react in three ways. First,



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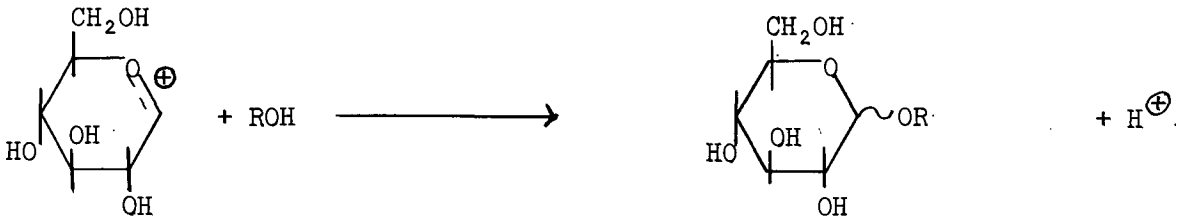
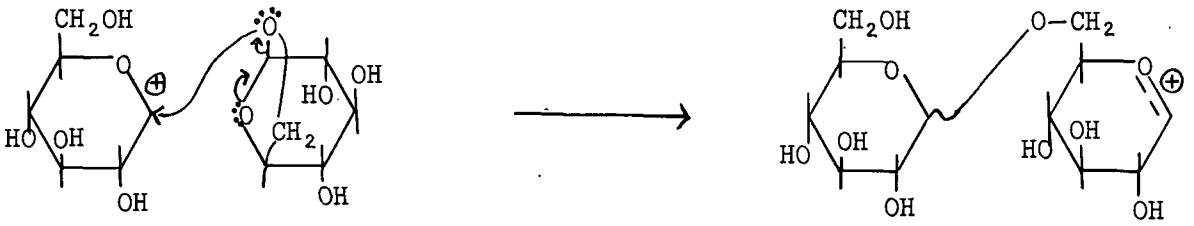
the ion can return to the protonated 1,6-anhydro-β-D-glucopyranose. Second, the ion can react with a free hydroxyl on another monomer molecule (ROH) to form a glycosidic bond and regenerate the protic catalyst. Third, the carbonium-oxonium ion can react



with the oxygen of the 1,6-anhydride bridge of another monomer molecule to form a (1→6)-linkage and regenerate the ion directly. Similar reactions have been proposed for the polymerization of cyclic ethers (15), which in the presence of Lewis acids,

*Ring opening of the C-5 ring-oxygen in the pyranose ring is considered less likely than ring opening of the 1,6-anhydride bridge since seven-membered rings are less stable than six-membered rings (1).



are believed to react by a trialkyloxonium ion mechanism. At present there is not enough information to enable differentiation between the mechanisms proposed by Schuerch, et al. (7, 9) and the ones proposed by Goldstein and Hullar (1).

STATEMENT OF THE PROBLEM

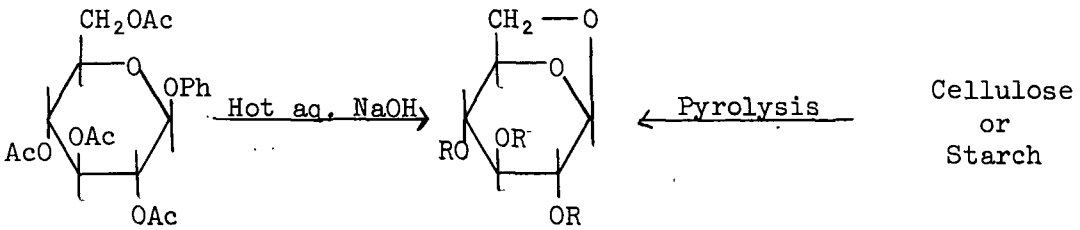
The protic acid-catalyzed polymerization of 1,6-anhydro-β-D-glucopyranose (I) was first reported one-half century ago; however, the mechanism of this reaction has not been resolved and is the topic under investigation in this thesis. In an attempt to resolve this mechanism, a number of 1,6-anhydrides structurally related to 1,6-anhydro-β-D-glucopyranose (I) were prepared and polymerized. The C-2, C-3, or C-4 hydroxyl group was either specifically blocked, replaced by a hydrogen atom or positioned different sterically. The relative rates of disappearance of monomer in the polymerization reaction were measured and this information used to propose a reaction mechanism.

RESULTS AND DISCUSSION

PREPARATION OF COMPOUNDS

Synthesis schemes for 1,6-anhydro sugars used in the thesis are presented. Three of these, 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II), 1,6-anhydro-4-O-methyl-β-D-glucopyranose (IV), and 1,6-anhydro-2,4-di-O-methyl-β-D-glucopyranose (VI), were prepared for the first time during the course of this work.

The preparation of 1,6-anhydro-β-D-glucopyranose (I, levoglucosan) may be accomplished through either the alkaline degradation of phenyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (Ia) or through the pyrolysis of cellulose or starch (16). For large-scale laboratory preparations the alkaline degradation route of



Ia

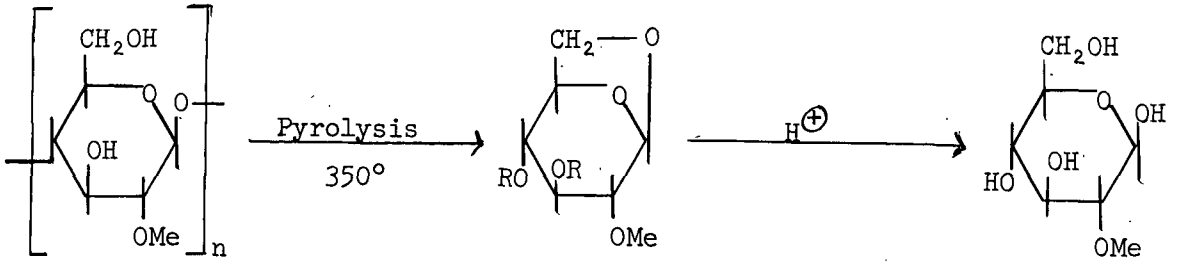
I R=H
Ib R=Ac

(I) is preferred, since the reported yield of (I) by the pyrolysis of starch is only 18% (16).

In this work the method of Coleman (17) was employed to synthesize (I). 1,2,3,4,6-Penta-O-acetyl-β-D-glucopyranose was reacted with phenol in the presence of a catalytic amount of p-toluenesulfonic acid monohydrate to give (Ia). Treatment of (Ia) with hot aqueous sodium hydroxide solution led to (I), which was purified through its readily crystallizable triacetate (Ib). Deesterification of (Ib) with sodium methoxide in methanol gave 1,6-anhydro-β-D-glucopyranose (I) in an overall yield of 50% from 1,2,3,4,6-penta-O-acetyl-β-D-glucopyranose.

1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II, 2-O-methyllevoglucosan), whose synthesis has previously not been reported, was prepared by two independent routes. The first route involves the pyrolysis of 2-O-methylcellulose (IIa) which was synthesized according to Falconer and Purves' procedure (18) in 47% yield, based on cellulose. The product (IIa), as described by these authors, was isolated in this work, and to the author's knowledge this is the first independent check on their procedure. Pyrolytic degradation of (IIa) at 350° and 0.02 mm. Hg produced an amber-colored, viscous distillate which, upon treatment with benzoyl chloride in pyridine, gave crystalline 1,6-anhydro-3,4-di-O-benzoyl-2-O-methyl-β-D-glucopyranose (IIb). Deesterification of (IIb) with sodium methoxide in a mixture of chloroform and methanol gave a crystalline, hygroscopic solid (II) in an overall yield of 16% based on cellulose. Compound (II) was identified through its nuclear magnetic resonance (NMR) spectrum and by its acid-hydrolysis which gave crystalline 2-O-methyl-β-D-glucopyranose (IIc).

The isolation of (II) from the pyrolysis of 2-O-methylcellulose may provide important information concerning the mechanism of the pyrolysis of cellulose (Appendix I).



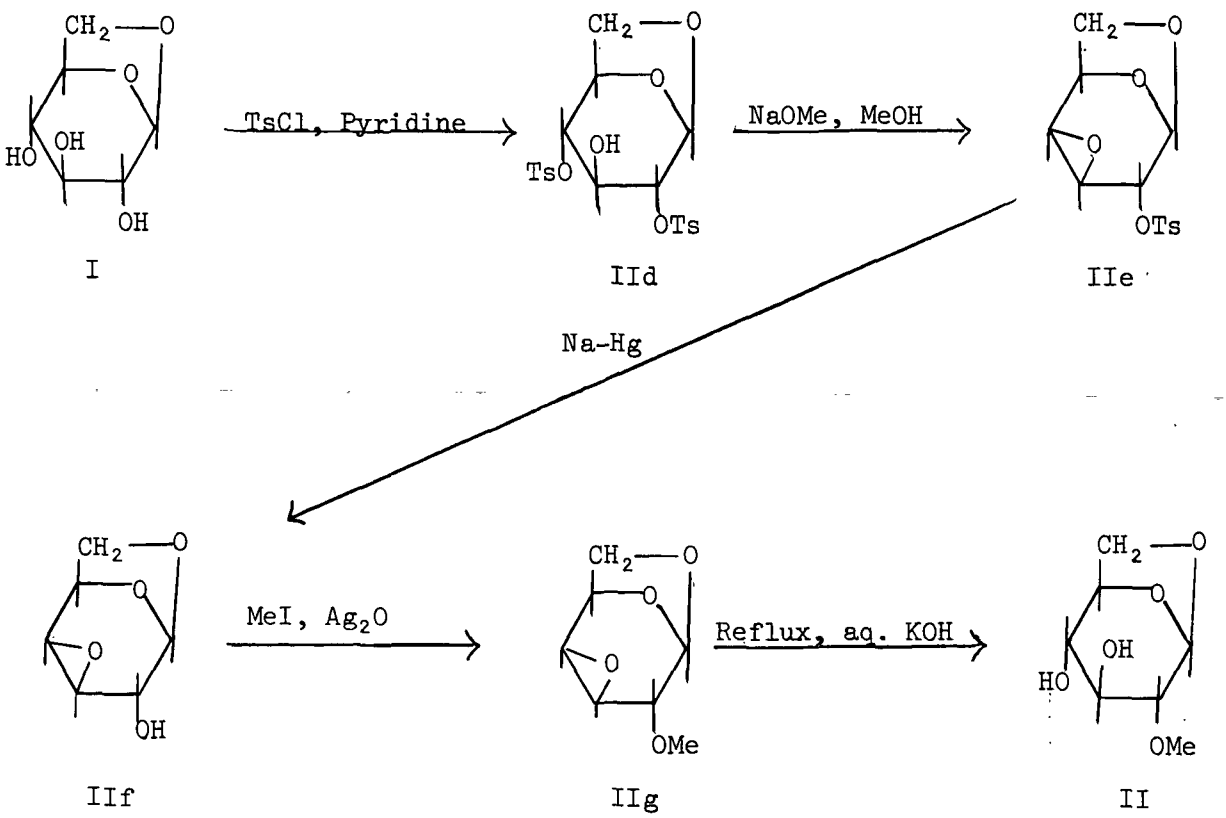
IIa

II R=H

IIb R=PhC(=O)-

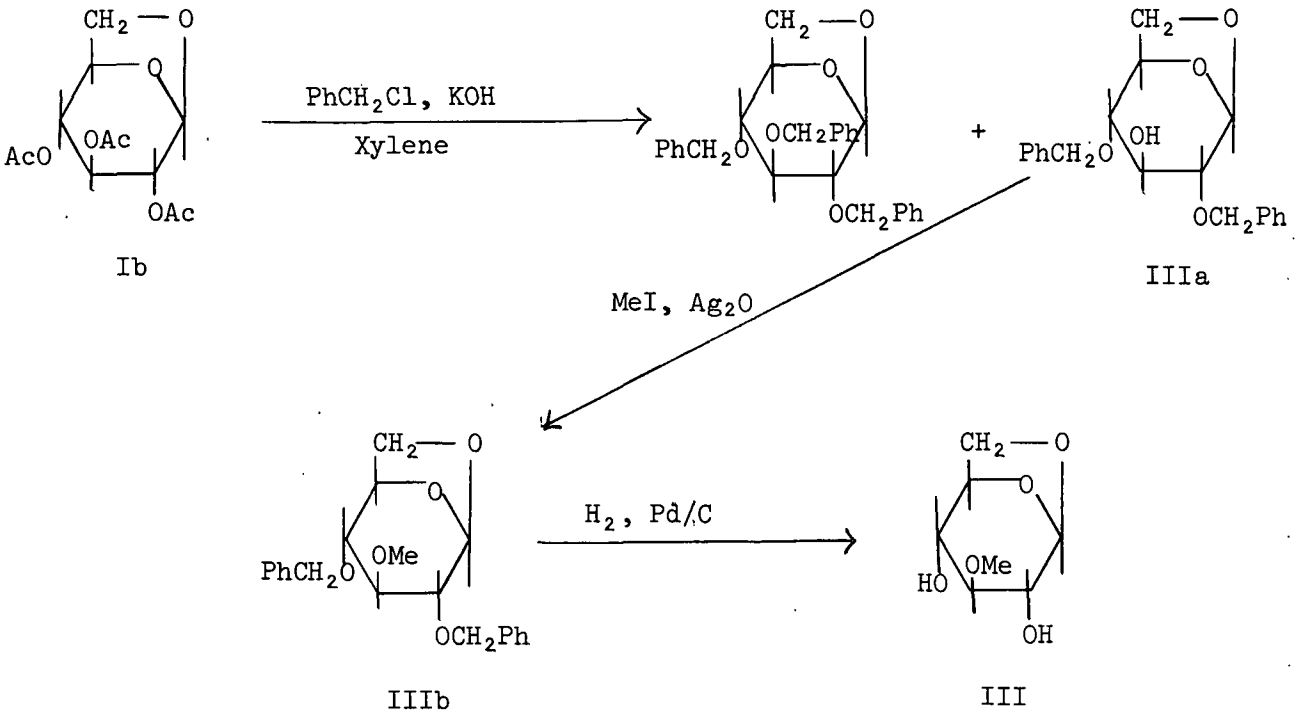
IIc

Compound (II) was also prepared by an alternate procedure in an overall yield of 20%, starting with 1,6-anhydro-β-D-glucopyranose (I). Using established procedures, (I) was converted to its 2,4-di-O-p-toluenesulfonate derivative (IId) by reaction of (I) with p-toluenesulfonyl chloride (TsCl) in pyridine (19). The sirupy product (IId) was reacted with sodium methoxide in methanol (19) to yield 1,6:3,4-dianhydro-2-O-p-toluenesulfonyl-β-D-galactopyranose (IIe). Removal of the tosyl group at the C-2 atom of (IIe) using sodium amalgam (20) gave 1,6:3,4-dianhydro-β-D-galactopyranose (IIf) which, after undergoing a Purdie methylation, afforded the known 1,6:3,4-dianhydro-2-O-methyl-β-D-galactopyranose (IIg) (21). Upon refluxing (IIg) in 1M aqueous potassium hydroxide, a compound was obtained in 71% yield that was identical to 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II) prepared by the pyrolysis of 2-O-methylcellulose (IIa).



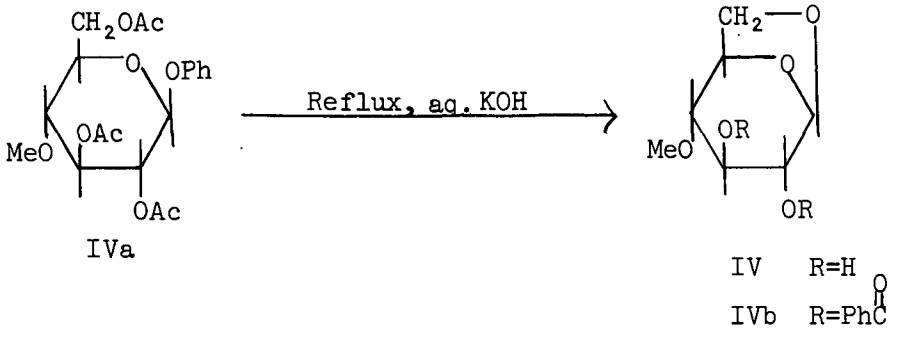
A single attempt was made to prepare 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II) in a one-step synthesis through the methylation of 1,6-anhydro-β-D-glucopyranose (I). There have been a number of reports where etherification and esterification of cellulose, starch, or methyl D-glucopyranosides leads to a predominance of substitution at the C-2 hydroxyl (22-26). Thus, (I) was methylated using a modified Haworth procedure (27) under conditions favoring formation of the monomethyl ethers, and the reaction products were separated by sorption column chromatography on silica gel. The composition of the monomethyl fraction was determined by NMR and the percent of the 2-, 4-, and 3-methyl ethers were found to be 54, 36, and 10%, respectively. Hence, the 2- and 4-hydroxyls are almost equally reactive, while the 3-hydroxyl is least reactive. Similar reactivities of these hydroxyl groups have been found with reactions using the reagents benzyl chloride (28), benzoyl chloride, and p-toluenesulfonyl chloride (29). Since the 2-hydroxyl was not selectively substituted and since the monomethyl ethers were difficult to separate, this method was least desirable for the preparation of (II).

1,6-Anhydro-3-O-methyl-β-D-glucopyranose (III, 3-O-methyllevoglucosan) was prepared by the method of Reeves (30). 2,3,4-Tri-O-acetyl-1,6-anhydro-β-D-glucopyranose (Ib) was reacted with benzyl chloride ($PhCH_2Cl$) and potassium hydroxide in xylene to give the tribenzyl and the 2,4-dibenzyl (IIIa) ether derivatives of (I) in 51 and 27% yields, respectively (28). Compound (IIIa) was methylated twice with silver oxide and methyl iodide to give sirupy 1,6-anhydro-2,4-di-O-benzyl-3-O-methyl-β-D-glucopyranose (IIIb). Removal of the benzyl groups from (IIIb) using hydrogen over palladium-on-carbon gave 1,6-anhydro-3-O-methyl-β-D-glucopyranose (III). The overall yield of (III) from the triacetyl derivative of 1,6-anhydro-β-D-glucopyranose (I) was 14%.



Ib IIIa IIIb III

The synthesis of 1,6-anhydro-4-O-methyl-β-D-glucopyranose (IV, 4-O-methyl-levoglucosan), which is a new compound, was accomplished in 61% yield by way of the intermediate phenyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranoside (IVa) (Appendix II). Compound (IVa) upon reaction in hot potassium hydroxide solution gave crystalline (IV). Benzoylation of (IV) with benzoyl chloride in pyridine gave the crystalline dibenzoate (IVb). The method of choice for the preparation of large quantities



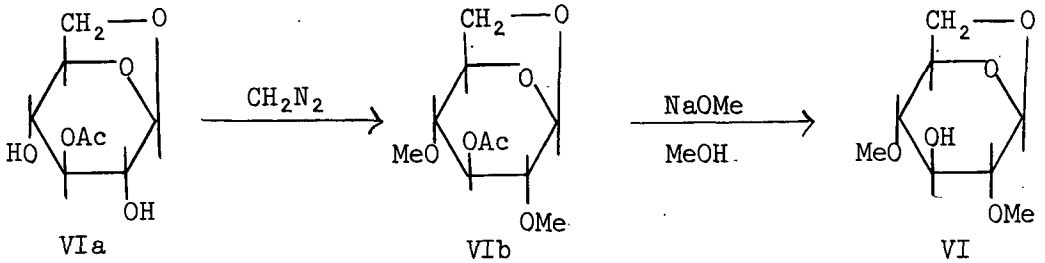
IVa

IV R=H

IVb R=PhC(=O)

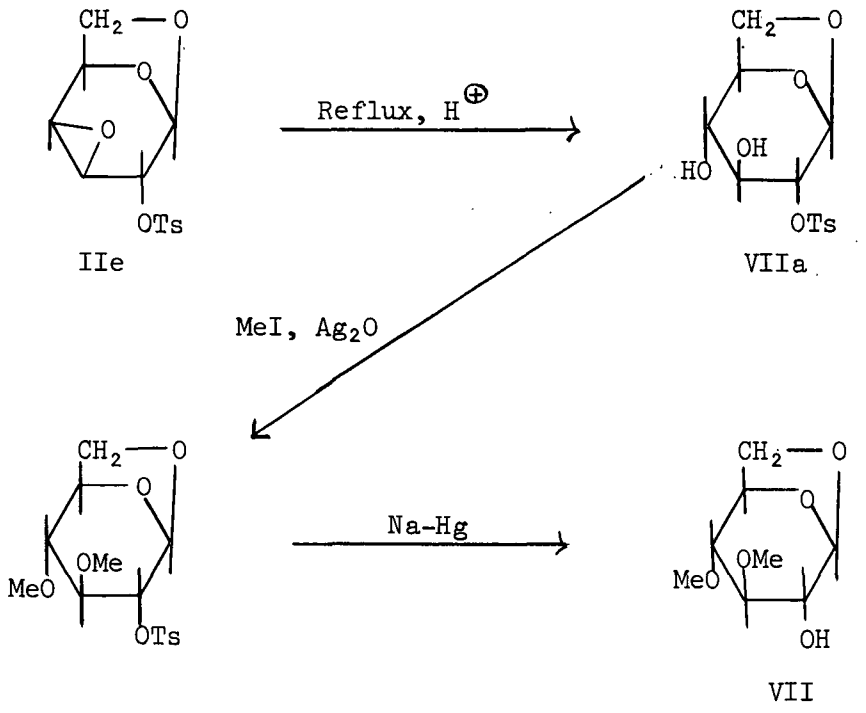
of the intermediate (IVa) involved methylation of phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (IVc) with methyl iodide and silver oxide in N,N-dimethylformamide. In addition to (IVa), phenyl 3,4,6-tri-O-acetyl-2-O-methyl-β-D-glucopyranoside was also formed in the etherification reaction. The position of the methyl group in 1,6-anhydro-4-O-methyl-β-D-glucopyranose (IV) was determined by NMR and by characterization of its precursor (IVa), which has not been reported in the literature. Compound (IVa) was identified by its preparation through two independent routes. The first route involved condensation of known 1,2,3,6-tetra-O-acetyl-4-O-methyl-β-D-glucopyranose (IVe) (31) with phenol, and the second route involved methylation of the 4-hydroxyl group on phenyl 2,3,6-tri-O-acetyl-β-D-glucopyranoside (IVf) (32) with diazomethane-boron trifluoride etherate reagent (31).

1,6-Anhydro-2,4-di-O-methyl-β-D-glucopyranose (VI, 2,4-di-O-methyllevoglucosan), whose preparation has not been reported, was synthesized in nearly quantitative yield from 1,6-anhydro-3-O-acetyl-β-D-glucopyranose (VIa) (33). Methylation of Compound (VIa) with diazomethane-boron trifluoride etherate reagent (31) gave crystalline 1,6-anhydro-3-O-acetyl-2,4-di-O-methyl-β-D-glucopyranose (VIb). De-esterification of (VIb) in the usual manner with sodium methoxide in methanol gave sirupy 1,6-anhydro-2,4-di-O-methyl-β-D-glucopyranose (VI). The structure assigned to (VI)is based on the method of synthesis and its NMR spectrum.

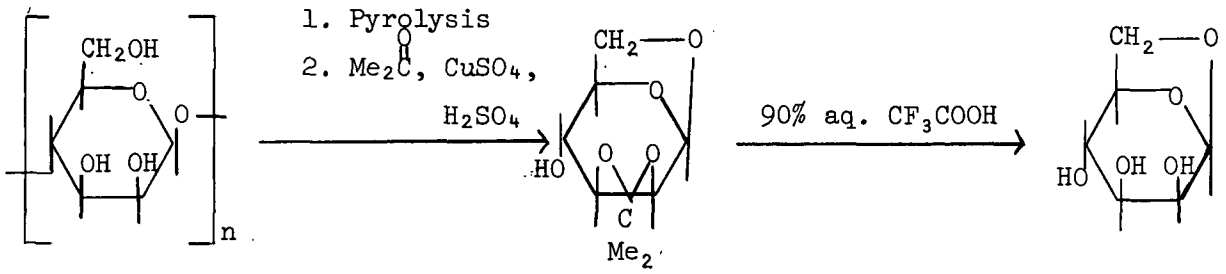


1,6-Anhydro-3,4-di-O-methyl-β-D-glucopyranose (VII, 3,4-di-O-methyllevoglucosan), previously reported (29) as a sirup, was isolated in crystalline form using a three-step synthesis starting from 1,6:3,4-dianhydro-2-O-p-toluenesulfonyl-β-D-galactopyranose

(IIe). Refluxing (IIe) in a four-to-one mixture of dioxane and 4.7M aqueous sulfuric acid solution for 45 min. preferentially opens the 3,4-epoxide to give a 76% yield of 1,6-anhydro-2-O-p-toluenesulfonyl-β-D-glucopyranose (VIIa) (34). Two successive Purdie methylations of (VIIa) followed by removal of the tosyl group with sodium amalgam in 80% aqueous methanol gave crystalline (VII) in an overall yield of 33%.



1,6-Anhydro-β-D-mannopyranose (IX, levomannosan) was prepared by the pyrolysis of ivory nut meal (35) which contains principally a β-1,4 linked mannan (IXa). The pyrolyzate was treated with a mixture of acetone, cupric sulfate, and a trace of concentrated sulfuric acid to give 1,6-anhydro-2,3-isopropylidene-β-D-mannopyranose (IXb) (36). Removal of the 2,3-ketal with 90% aqueous trifluoroacetic acid solution (37) gave 1,6-anhydro-β-D-mannopyranose. The overall yield of (IX) from the ivory nut meal was 5.8%.



IXa IXb IX

The following compounds used in the thesis were supplied through the courtesy of Dr. Paul A. Seib: 1,6-anhydro-2,3-di-O-methyl-β-D-glucopyranose (V, 2,3-di-O-methyllevoglucosan) (38), 1,6-anhydro-2,3,4-tri-O-methyl-β-D-glucopyranose (VIII, trimethyllevoglucosan) (39), 1,6-anhydro-2-deoxy-β-D-arabino-hexopyranose (X, 2-deoxylevoglucosan) (40), 1,6-anhydro-β-D-galactopyranose (XII, levogalactosan) (9), 1,6-anhydro-2-O-methyl-β-D-galactopyranose (XIII, 2-O-methyllevogalactosan) (9, 41), 1,6-anhydro-4-O-methyl-β-D-mannopyranose (XIV, 4-O-methyllevomannosan) (30), and 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-glucopyranose (XIa) (42). Deacetylation of (XIa) with sodium methoxide in methanol gave 1,6-anhydro-4-O-(β-D-glucopyranosyl)-β-D-glucopyranose (XI, cellobiosan) (42).

POLYMERIZATION INVESTIGATION

The 1,6-anhydrides I-IV, VII, and IX-XIII, were heated in sealed glass tubes in the presence of monochloroacetic acid (MCA) at 115°. The mole ratio of 1,6-anhydride to MCA ranged from 54:1 to 51:1. A series of polymerization tubes was used for a kinetic run with each 1,6-anhydride. The monomer remaining after heating a tube for a given period was determined by trimethylsilylation of the reaction mixture and quantitative analysis of the monomer's trimethylsilyl ether by gas-liquid chromatography (GLC). The weight fraction of unreacted monomer (F_M) for each 1,6-anhydride is plotted against time in Fig. 1 and 2. A semilogarithmic plot of the

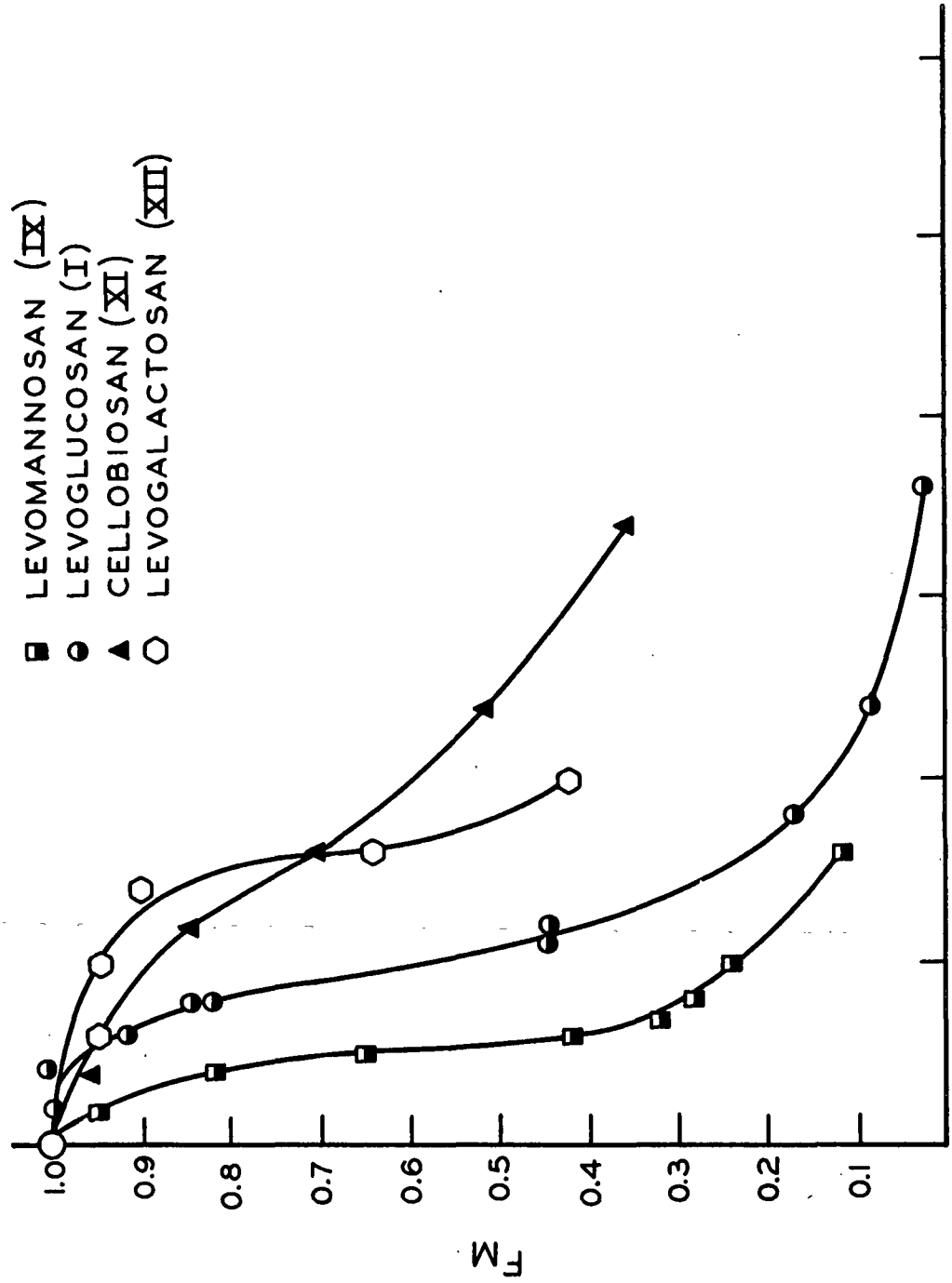


Figure 1. Disappearance of Monomer in the Polymerization of 1,6-Anhydrides

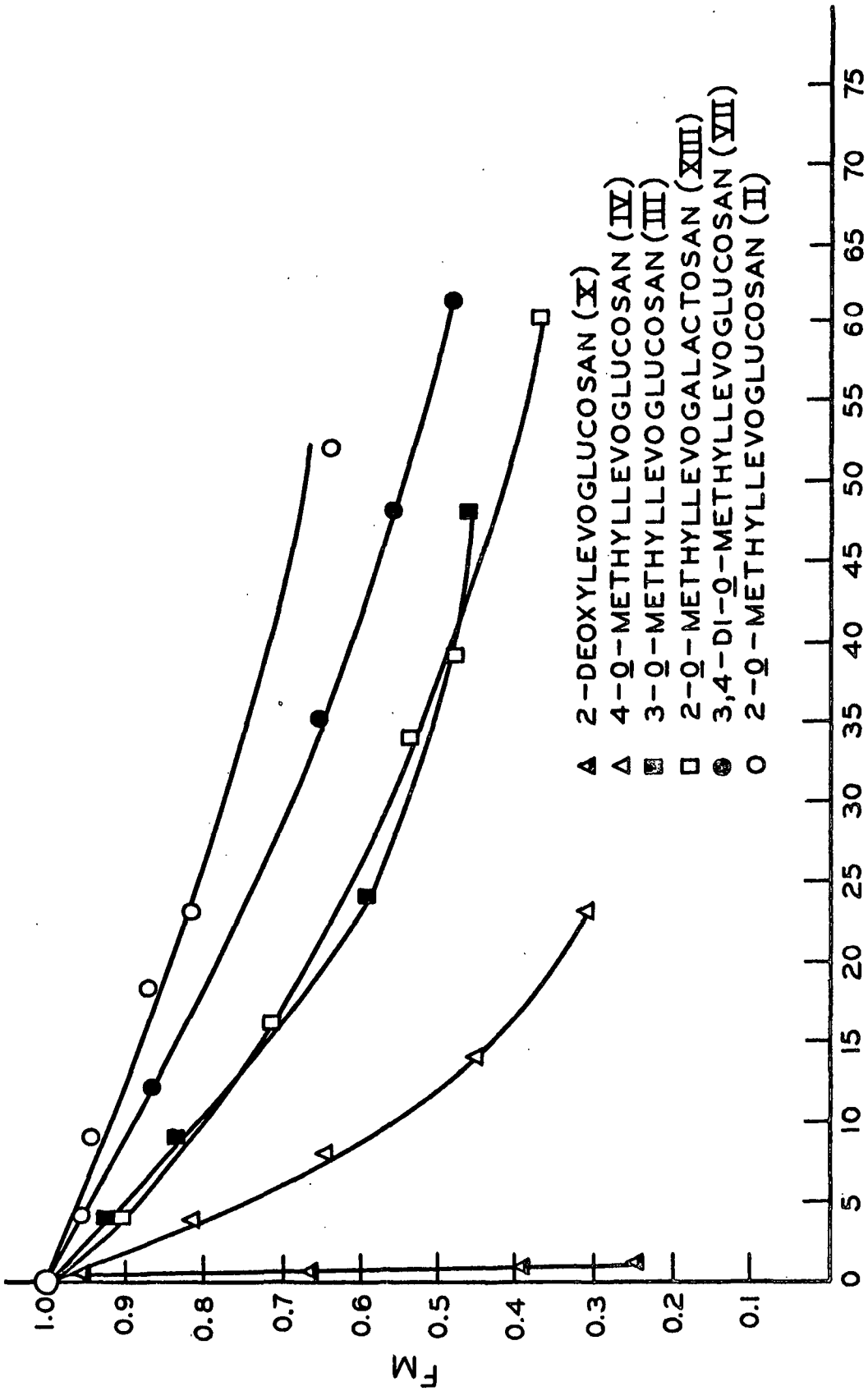


Figure 2. Disappearance of Monomer in the Polymerization of 1,6-Anhydrides

data is given in Fig. 3 and 4. The reproducibility of the F_M values was checked by several independent polymerizations of (I) and found to be $\pm$ 3%.

As seen in Fig. 1-4, the disappearance of a 1,6-anhydride followed one of two patterns. One type of disappearance pattern is typified by the behavior of 1,6-anhydro-β-D-glucopyranose (I). During the early stages of heating at 115°, (I) (m.p. 179-80°) disappears very slowly because of the heterogeneity of the reaction mixture. After a homogeneous melt is obtained, the monomer is consumed by a pseudo first-order reaction. 1,6-Anhydro-β-D-mannopyranose (IX) (m.p. 210-11°) and 1,6-anhydro-β-D-galactopyranose (XII) (m.p. 223-4°) behave the same as (I). The remaining 1,6-anhydrides, which all had melting points below 115°, formed a homogeneous melt in a very short period of time. These 1,6-anhydrides disappear immediately upon heating by a pseudo, first-order reaction. 1,6-Anhydro-4-O-(β-D-glucopyranosyl)-β-D-glucopyranose (XI) initially does not disappear by a first-order reaction, but does so after $F_M \approx 0.9$.

The reaction order for the polymerization of each monomer was determined by the graphical procedure of Wright, et al. (43), which is an accurate method for determining reaction orders between 0 and 2.5. For the disappearance of the 1,6-anhydrides, with the exception of 1,6-anhydro-β-D-galactopyranose (XII), the reaction orders were found in the range of 0.7 to 1.4. For compound (XII) the polymerization data were too scattered to prevent an accurate determination of the reaction order.

With prolonged heating, the rate of disappearance of monomer began to deviate from first-order kinetics. This effect was noticed for several 1,6-anhydrides whenever the monomer was heated beyond one half-life of the monomer (Fig. 3 and 4). It is believed the reaction decelerates for two reasons. First, the monochloroacetic acid (MCA) catalyst is lost during the reaction, probably through self-catalyzed esterification with sugar hydroxyl groups (44). The results of the titrimetric

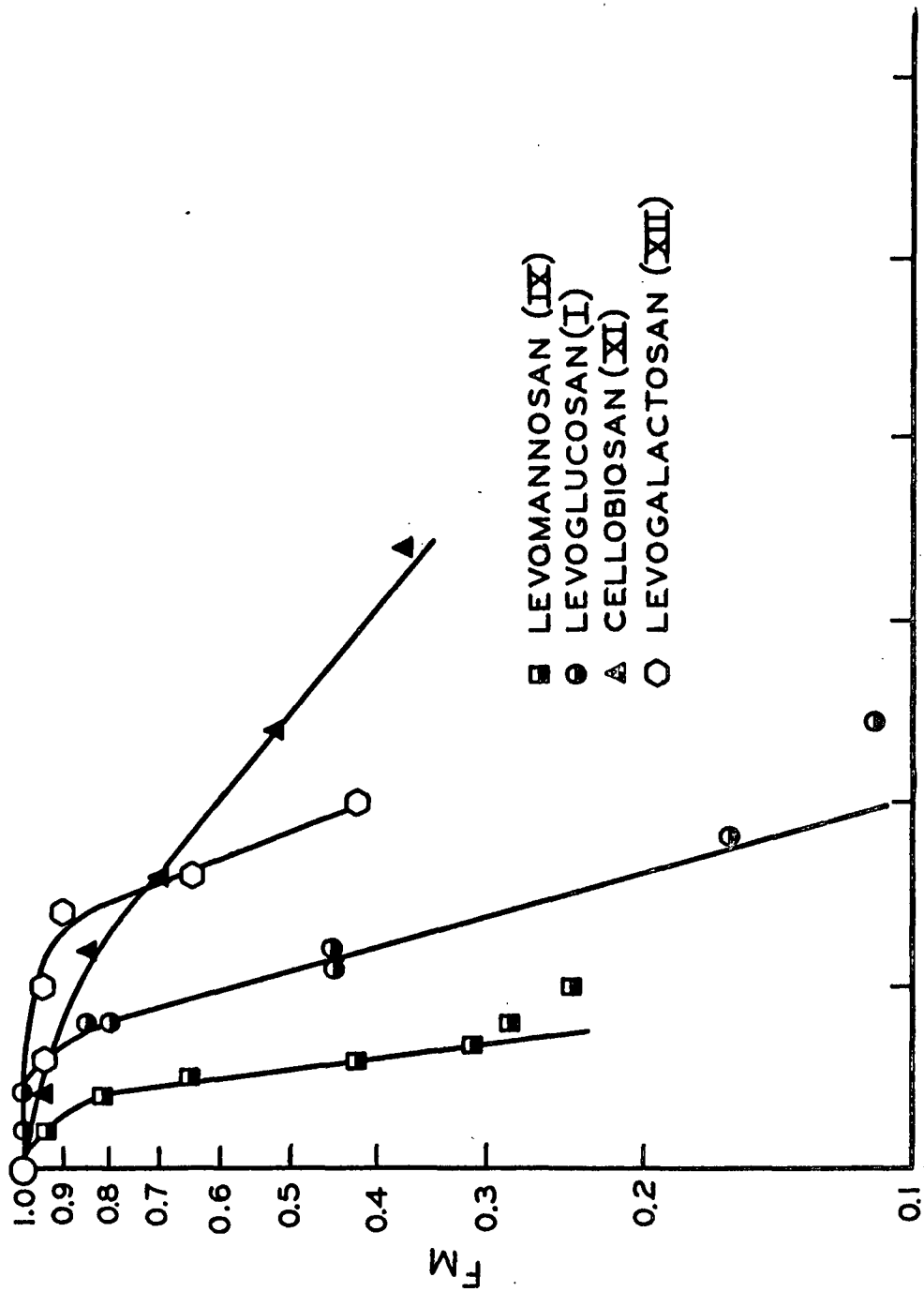


Figure 3. Pseudo First-Order Plots for Disappearance of Monomer in the Polymerization of 1,6-Anhydrides

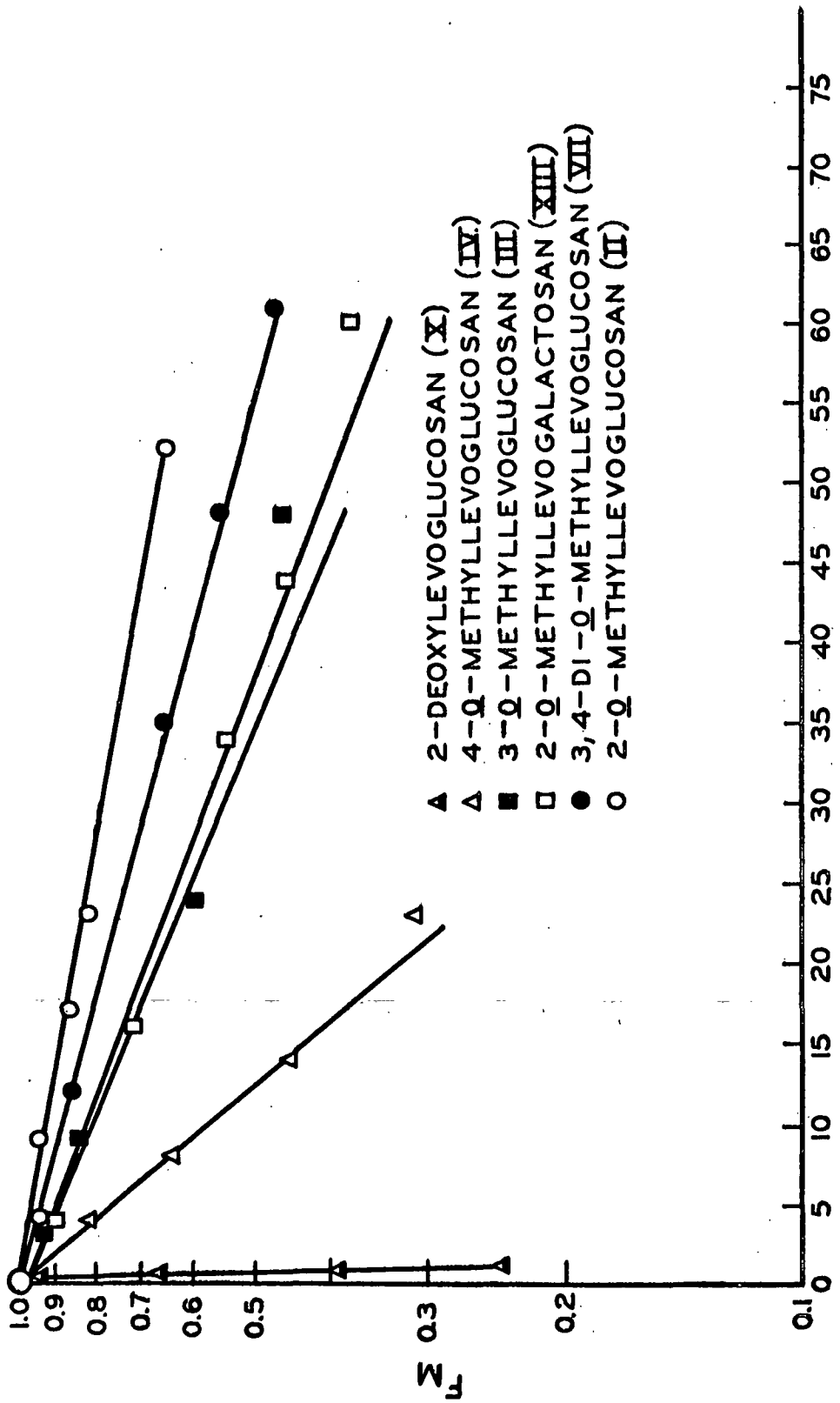


Figure 4. Pseudo First-Order Plots for Disappearance of Monomer in the Polymerization of 1,6-Anhydrides

determination of acid remaining in the MCA-catalyzed polymerization of (I) are given in Table I. It was shown in a separate experiment that 1,6-anhydro-β-D-glucopyranose (I) in the absence of MCA does not polymerize at 115°; 99% of the monomer was recovered after heating 24 hr.

TABLE I

FRACTION OF REMAINING MCA AND FRACTION OF REMAINING MONOMER IN THE POLYMERIZATION OF 1,6-ANHYDRO-β-D-GLUCOPYRANOSE

Polymerization Time, hr.	F_M [a]	F_{MCA} [b]
3.0	0.92	0.98
4.0	0.82	1.00
4.7	0.68	0.98
6.1	0.43	0.95
16.0[c]	0.02	0.61
16.0[c]	0.02	0.57
16.0[c]	0.02	0.58

[a] Determined from polymerization curve (Fig. 1).

[b] Fraction remaining MCA which has been corrected for catalyst loss (3-5%) during preparation of polymerization tubes (see Determination of Catalyst Loss, p. 77).

[c] Triplicate experiments.

Since the loss of catalyst is much slower than the loss of monomer, the rates of monomer disappearance are not noticeably affected during the early stages of polymerization. However, the loss of catalyst is rather severe with prolonged heating, and nearly 42% of MCA is lost when the fraction of (I) remaining in the melt equals 0.02. This amount of catalyst loss would certainly slow down the polymerization reaction. Schuerch, et al. (7) has found that a 50% reduction of the catalyst concentration gave nearly a 50% reduction in the amount of polymer.

The second reason that the rate of disappearance of monomer begins to deviate from pseudo, first-order kinetics is due to the decrease in reactivity of the 1,6-anhydro bridge with substitution on the ring hydroxyls. This factor is discussed in detail later in this section (p. 29).

All polymerization reactions were examined chromatographically when each monomer had been heated for approximately one half-life. At this time, all the reaction products were amber-colored glasses. Acid-catalyzed dehydrations of sugars gives furan derivatives (45) which condense to form highly colored products. Thin-layer and paper chromatography showed no products with a mobility higher than the original monomer, as might be expected if the 1,6-anhydro sugar is dehydrated.

The principal reaction products formed from 1,6-anhydro-β-D-glucopyranose at F_M = 0.5 were in the same zone of the paper chromatogram as cellobiosan and 1,6-anhydro-4-O-(α-D-glucopyranosyl)-β-D-glucopyranose (maltosan), although some reaction products remained close to the starting line. The products from (I) were not well resolved in this zone; thin-layer chromatograms showed three distinct spots together with some streaking, indicating that the 1,6-anhydrodisaccharide fraction probably contains at least three of the six possible 1,6-anhydrodisaccharides. Analysis by GLC of the trimethylsilylated reaction mixture confirmed the presence of cellobiosan and maltosan. Products with low R_G values were also observed in the polymerization mixtures obtained at F_M = 0.5 for all other 1,6-anhydrides.

The slowest reacting monomer, 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II), was heated 16 days at 115°, and 37% of the product was precipitated from a 3.1% aqueous solution by the addition of five volumes of acetone. The polymeric material had a number-average molecular weight of 1,030 as determined by vapor-pressure osmometry. The specific rotation of the polymer was +79.2°, indicating the presence

of both α- and β-D-glycosidic linkages (1). The synthetic 2-O-methyl-D-glucan was hydrolyzed to give a sirup whose product, as evidenced by paper chromatography, was 2-O-methyl-D-glucopyranose.

The fastest reacting monomer, 1,6-anhydro-2-deoxy-β-D-arabino-hexopyranose (X) was heated for 4 hr. at 115° and gave a 58% yield of polymeric material which was precipitated from an 0.8% aqueous solution by the addition of 3 volumes of acetone. Hydrolysis of the polymeric substance followed by acetylation of the polymer hydrolyzate gave crystalline 1,3,4,6-tetra-O-acetyl-2-deoxy-α-D-arabino-hexopyranose.

Since all monomers in a homogeneous melt disappear initially by a first-order process to give compounds of higher molecular weight, a comparison of the rates of disappearance gives a measure of each monomer's tendency to form a polysaccharide. The pseudo, first-order rate constants of the model compounds are the graphically determined slopes of the linear portion of the semilogarithmic plots shown in Fig. 3 and 4. These rate constants are estimated to be accurate to within a factor of two and are compiled in Table II, along with the relative rates in reference to the slowest reacting monomer, 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II). The densities of all monomer melts are assumed identical.

The data in Table II are best explained by assuming that 1,6-anhydro-β-D-glucopyranose (I) polymerizes according to the mechanism which is similar to the one proposed by Goldstein and Hullar (1) (Fig. 5). The first step in this reaction mechanism is a rapid, equilibrium-controlled, protonation of (I) at the oxygen atom between the C-1 and C-6 atoms to form the conjugate acid. The conjugate acid then undergoes heterolytic cleavage, probably without assistance by the 2-hydroxyl group (p. 30), in the rate-controlling step to give a carbonium-oxonium ion intermediate ($\underline{M}^{\oplus}$). This intermediate then reacts with a hydroxyl group to produce a dimer with

regeneration of the protic catalyst. The dimer molecule which contains a reactive 1,6-anhydro bridge may now undergo a series of reactions analogous to the monomer reactions to give trimer.

TABLE II

PSEUDO FIRST-ORDER RATE CONSTANTS FOR THE ACID-CATALYZED POLYMERIZATION OF 1,6-ANHYDRIDES

1,6-Anhydro Sugar	Pseudo Rate Constant k, $hr.^{-1}$	Relative Rate[a]
2-Deoxylevoglucosan (X)	2.1	240
Levomannosan (IX)	0.78	91
Levoglucosan (I)	0.32	37
Levogalactosan (XII)	0.15	17
Cellobiosan (XI)	0.077	9.0
4-O-Methyllevoglucosan (IV)	0.054	6.3
3-O-Methyllevoglucosan (III)	0.022	2.6
2-O-Methyllevogalactosan (XIII)	0.020	2.3
3,4-Di-O-methyllevoglucosan (VII)	0.012	1.4
2-O-Methyllevoglucosan (II)	0.0086	1.0

[a]Rate with respect to 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II).

The observance of the near pseudo, first-order kinetics for much of the disappearance of (I) and the other 1,6-anhydrides can be explained by one of two limiting cases. In the first case, the reactivity of the 1,6-anhydro bridge remains constant and is independent of the polymers chain length.* In the second case, the

*Flory (46, 47) established that the rate of esterification of aliphatic acids is independent of the chain length. However, the reactivity of higher molecular weight species may not be the same as lower molecular weight species in systems where steric or conformational factors change with molecular weight (46).

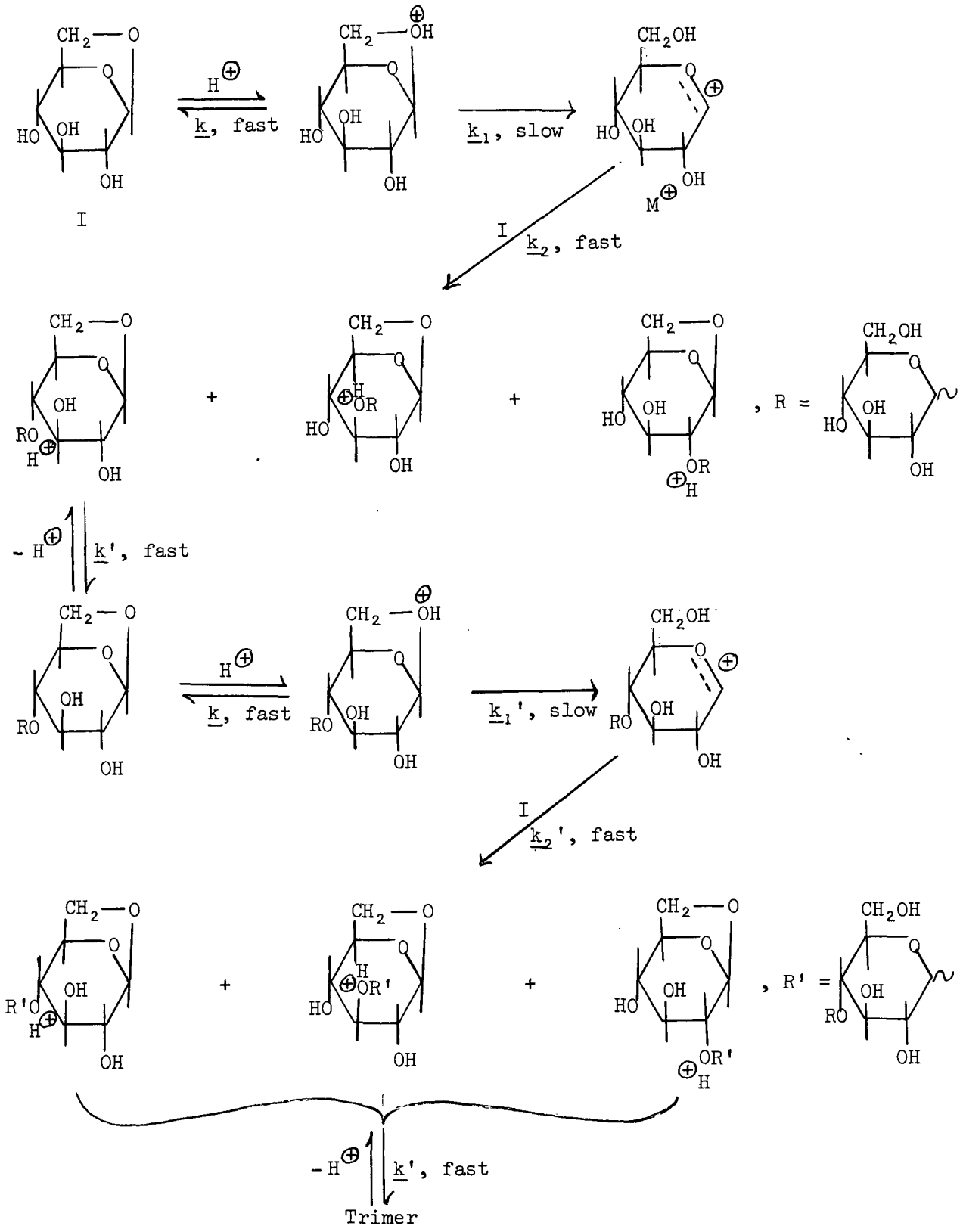


Figure 5. Proposed Mechanism for the Acid-Catalyzed Polymerization of 1,6-Anhydro-β-D-glucopyranose (I)

1,6-anhydro bridge of a dimer or higher molecular weight oligomer is much less reactive than the 1,6-anhydro bridge of the monomer. For both cases, monomer disappears initially to give only dimers. However, with a build-up of dimer fraction in the first case, monomer will also begin to disappear by its hydroxyl groups reacting with the 1,6-anhydro bridge of a dimer; such a route for the disappearance of monomer molecules would not be open in the latter case where $\underline{k}_1'$ is very much smaller than $\underline{k}_1$ (Fig. 5).

In the second case, if $\underline{k}_2$ is much greater than $\underline{k}_1$, the amount of reactive ion ($\underline{M}^{\oplus}$) will be very small and can be neglected from the rate expression. The rate of monomer disappearance can be formulated by the pseudo, first-order rate Equation (2).

$$dM/dt = -2 \cdot k_1 \cdot K \cdot M \qquad (1)$$

$$dM/dt = -k_{pseudo} \cdot M \qquad (2)$$

where

$\underline{dM}/\underline{dt}$ = rate of monomer disappearance, moles/liter hr.$^{-1}$

$\underline{k}_1$ = rate constant for rate-controlling step, hr.$^{-1}$

$\underline{K}$ = equilibrium constant for I and its conjugate acid

$\underline{M}$ = monomer concentration, moles/liter

$\underline{k}_{pseudo} = 2 \cdot \underline{k}_1 \cdot \underline{K}$

In this second case, where 1,6-anhydro reactivity decreases with substitution on the hydroxyl groups of the 1,6-anhydride, Equation (2) must eventually lose its validity as $\underline{F}_{\underline{M}}$ goes to a smaller and smaller value. Prior to the build-up of dimer in the polymerization melt, each activated monomer unit ($\underline{M}^{\oplus}$) must react with another molecule of I. However, as the amount of oligomer increases in the reaction melt the activated monomer unit ($\underline{M}^{\oplus}$) will have a greater probability of reacting with

hydroxyl groups on higher molecular weight material. In the limiting situation where $\underline{M}^{\oplus}$ can only react with the hydroxyl groups of oligomer, because monomer is in very low concentrations, the factor of two in Equation (1) would become unity.

Although these two cases could not be distinguished by the shapes of the curves in the pseudo, first-order plots presented in this work*, evidence indicates that 1,6-anhydro-β-D-glucopyranose (I) and its derivatives disappear in a manner more closely associated with the second case than the first case. The direct evidence for the second case, which states there is decreased reactivity of a 1,6-anhydro bridge of an oligomer in contrast to monomer, is provided by the fact that cellobiosan reacts at approximately one-fourth the rate of I (Table II). Methoxyl substitution on the C-4 atom of I is almost equally detrimental to the reactivity of the 1,6-anhydro bridge. Substitution at the C-4 atom in comparison to the C-2 and C-3 atoms of I has the smallest effect on the 1,6-anhydride reactivity (Table II). Since (1→3)-linked and especially (1→2)-linked dimers would be expected (1) to constitute at least half the 1,6-anhydrodisaccharide fraction in the polymerization of I, the overall rate constant (k_1') for dimer disappearance would probably be less than the rate constant found for cellobiosan.

This decrease in the reactivity of ether derivatives of I (1/4 to 1/37 as reactive as I) is not due to inductive or field effects since a methoxyl and a hydroxyl group have identical Charton polar substituent constants (48). The phenomenon may be explained as follows. The rate-controlling step of the reaction is the heterolysis of the 1,6-anhydride's conjugate acid to form a carbonium-oxonium ion in a half-chair conformation (Fig. 5). The conversion of the chair to the half-chair conformation requires at least rotation of the C-2 to C-3 and C-4 to C-5 bonds. An increase in

*In principle, the two cases should be distinguishable kinetically. For the case of constant reactivity, a first-order plot of monomer should be linear for all values of M/M_o (46). For the other case, the plot should be linear initially but eventually becomes curvilinear. Although a discontinuity was found in the plots presented in Fig. 3 and 4, another factor, catalyst consumption at longer reaction times was also operating to slow down the reaction.

the size of the groups attached to these positions will increase the hindrance to this conformational change (49), and will raise the energy of the transition state. On the other hand, the ground state energy of the methyl ether derivative of I is probably close to that of I, since the conformational energies of an hydroxyl and an O-alkyl group are practically identical (50, 51). The net effect is a larger energy requirement to the transition state for the ether derivatives of I and, therefore, these derivatives polymerize more slowly than I. Similar reasoning would explain the sluggish reactivity of 1,6-anhydro-2-O-methyl-β-D-galactopyranose.

This explanation of the polymerization reactivity of 1,6-anhydro-β-D-glucopyranose derivatives was adopted from the hypothesis of Edward (49), who first used this argument to account for some of the differences in the rates of acid hydrolyses of pyranosides. The hypothesis of Edward probably applies to the polymerization of I, since the mechanism of the hydrolysis of pyranosides is the same as shown in Fig. 5, except the reactive intermediate adds a molecule of water during hydrolysis instead of monomer. As might be expected, methyl ethers of methyl D-glucopyranosides hydrolyze more slowly than the parent glucopyranoses. De and Timell (52) found that the 2-, 3-, 4-, and 6-O-methyl derivatives of methyl β-D-glucopyranosides are hydrolyzed somewhat more slowly than the unsubstituted compound (Table III). These workers attribute these decreases to an increased hindrance when these molecules assume their transition state. The rotational effects should be additive. Thus, the permethylated glucopyranosides hydrolyze even more slowly relative to the unsubstituted glucopyranosides (53) than do the monomethyl derivatives. The trimethyl ether of I is also hydrolyzed more slowly than I (54) (Table III).

A reduction in eclipsing interaction at the C-2 to C-3 bond has been used to explain, in part, the enhanced acid-lability of methyl 2-deoxy-α-D-*arabino*-hexopyranoside and methyl 3-deoxy-α-D-*ribo*-hexopyranoside (55). It has been estimated

that rotational effects account for a factor of 20 in an overall difference of 2,000 between the rates of hydrolysis of methyl 2-deoxy-α-D-arabino-hexopyranoside and methyl α-D-glucopyranoside (1, 55). This same factor apparently explains why 1,6-anhydro-2-deoxy-β-D-arabino-hexopyranose (X) polymerizes 6.5 times faster than 1,6-anhydro-β-D-glucopyranose (I).

TABLE III

PSEUDO FIRST-ORDER RATE CONSTANTS FOR THE ACID-HYDROLYSIS OF METHYL β-D-GLUCOPYRANOSIDE AND SEVERAL OF ITS ETHER DERIVATIVES

Pyranoside	Pseudo Rate Constant x 10^{-2}, $hr.^{-1}$
[a]Methyl β-D-glucoside	3.75
2-Methyl ether	3.13
3-Methyl ether	3.39
4-Methyl ether	2.98
6-Methyl ether	2.33
[b]Methyl β-D-glucoside	6.9
Tetramethyl ether	2.3
[c]Levoglucosan	4.14
Trimethyl ether	0.6

[a]De and Timell (52). In 0.5M sulfuric acid solution at 70°, 0.025M glucoside solution, polarimetry.

[b]Haworth and Hirst (53). In 0.01M hydrochloric acid at 95-100°, polarimetry.

[c]Freudenberg, et al. (54). In 0.5M sulfuric acid solution at 70°, 0.2M glucoside solution, polarimetry.

The ability of compound (X) to form polymer indicates that the polymerization of 1,6-anhydro-β-D-glucopyranose (I) does not necessarily go by way of a 1,2-anhydro intermediate. Such an intermediate has been proposed by Bhattacharya and Schuerch (9) to explain the large decrease in the rate of polymerization of 1,6-anhydro-2-O-methyl-β-D-galactopyranose (XIII), which, in contrast to the unsubstituted compound

(XII) cannot form a 1,2-anhydro intermediate. These authors state:

> It appears that attack by the 2-hydroxyl group on the anhydro ring is an important part of the initiation process. This should not be considered as a means of assisting the ionization of the C-1 position, for Winstein, et al. (56) have shown that neither a neighboring methoxyl nor hydroxyl participate very much in the formation of a carbonium ion. Rather, it should be considered as an interconversion of a relatively unreactive protonated 1,6-anhydro ring to a relatively reactive 1,2-anhydro ring. When the 2-position is methylated, this transformation is not possible, and the polymerization is severely inhibited.

It is not likely that a 1,2-anhydro intermediate is involved in the polymerization of I and the other 1,6-anhydrides, provided anchimeric assistance by a 2-hydroxyl group can be ruled out (see below). The heterolyses of the conjugate acids of I and its 2-methyl ether are the rate-limiting steps of the polymerization reactions. The reactive intermediate formed from I may be partly or totally converted to a protonated 1,2-anhydro intermediate; however, this conversion would occur after the rate-controlling step. Even if a hydroxyl group on the C-2 atom leads eventually to a 1,2-anhydro intermediate and a methoxyl group blocks 1,2-anhydro formation, there should be little difference in the rates of reaction of I and its 2-methyl ether. Formation of a 1,2-anhydro intermediate from I but not from II, however, might be detectable in the stereochemistry of the glycosidic linkages formed during the polymerization of I and its 2-methyl ether. Since anomerization does not occur under the conditions of polymerization* (7), the optical rotations of the two polymers can yield useful information on the structure of the reacting intermediate. If 1,6-anhydro-β-D-glucopyranose (I) reacts through a 1,2-anhydro intermediate and its 2-methyl ether does not, the D-glucan should contain more β-linkages than the 2-O-methyl-D-glucan since Brigl's anhydride, 3,4,6-tri-O-acetyl-1,2-anhydro-α-D-glucopyranose reacts with alcohols in

*The optical rotations in water for the dextrans numbered 20A, 34, 36, and 37, which all have different polymerization times [see Table I in Ref. (7)], are +91 ± 5°.

the presence of trace amounts of acids to give a predominance of β-D-glucopyranosides (57, 58). The specific rotation of the D-glucan, $[\alpha]_D$ +91 ± 5° (7), indicates that it contains approximately the same or even fewer β-linkages than the 2-O-methyl-D-glucan, $[\alpha]_D$ +79.2°.

Anchimeric assistance by an hydroxyl and not a methoxyl in the heterolytic cleavage of the conjugate acid is probably not the reason why 2-substituted 1,6-anhydrides polymerize slowly. As seen in Table II, the 3-methyl and the 3,4-dimethyl ethers of I react almost as slowly as the 2-methyl ether even though the former derivatives contain free hydroxyls at C-2. Furthermore, the more rapid polymerization of 1,6-anhydro-β-D-mannopyranose (IX) compared to I is difficult to rationalize if anchimeric assistance to form an ion occurs by way of a 2-hydroxyl group. The 2-hydroxyl group in IX cannot assume a 1,2-trans diaxial orientation with the leaving group (O-6) on the C-1 atom. Therefore, assistance cannot occur in IX, yet it polymerizes more rapidly than 1,6-anhydro-β-D-glucopyranose (I), wherein the assisting and leaving groups are locked in optimum position for assistance.

In the polymerization of 1,6-anhydro-β-D-glucopyranose (I) using the catalyst monochloroacetic acid, it was concluded that:

1. Replacement of any of the hydroxyl groups in 1,6-anhydro-β-D-glucopyranose (I) by a methoxyl group or by a glucopyranosyl group at the C-4 atom decreases the rate of disappearance of the 1,6-anhydride whereas replacement by a hydrogen atom results in acceleration of the polymerization rate;
2. The effect of substitution on the rate of polymerization suggests this reaction is mechanistically related to the acid-hydrolysis of pyranosides; and

3. The polymerization data for several 1,6-anhydrides do not support the hypothesis of Schuerch, et al. (7, 9) that a 1,2-anhydro intermediate is required in the polymerization of 1,6-anhydro-β-D-glucopyranose (I).

NUCLEAR MAGNETIC RESONANCE INVESTIGATION

The monomethyl ether derivatives of 1,6-anhydro-β-D-glucopyranose (I) employed in the polymerization study were identified, in part, using nuclear magnetic resonance (NMR). A closer examination of the spectral data for these ethers revealed that a good correlation exists between the shifts of the ring protons and the position of methoxyl substitution. Based on the work reported herein, empirical rules were formulated from the proton resonances of the three monomethyl ether derivatives, and these rules were used successfully to predict (a) the chemical shifts of all the ring protons in the dimethyl and trimethyl ether derivatives of I and (b) the chemical shifts for certain protons in 1,6-anhydro-2-O-methyl-β-D-galactopyranose (XIII) and 1,6-anhydro-4-O-methyl-β-D-mannopyranose (XIV). This approach could be used in the future to correlate the chemical shifts of the methyl ethers of other 1,6-anhydrohexopyranoses, all of which contain the conformationally rigid 1-C(D) chair in the bicyclic [3.2.1] ring system (30, 59). In this manner, additional rules could be formulated to handle the changes in chemical shifts of ring protons expected when one or more hydroxyls on the chair form of any pyranoid sugar are methylated. Lemieux and Stevens (60) investigated the NMR spectra of several aldopentopyranoses and aldohexopyranoses, and they devised a set of rules to relate the chemical shifts of the ring protons with the orientation of hydroxyl groups around the ring. Recently, Heyns and Weger (59) studied the NMR spectra of the unsubstituted 1,6-anhydro-β-D-hexopyranoses and obtained a set of rules similar to those for the aldopentopyranoses and aldohexopyranoses.

In this work, the NMR spectra of 1,6-anhydro-β-D-glucopyranose (I) and its methyl ethers (II-VIII) were measured at 60 MHz in both methyl sulfoxide-$\underline{d}_6$ with tetramethylsilane (TMS) as the internal standard and in deuterium oxide with sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS) as the internal standard (Fig. 9-24, Appendix III). The chemical shifts of the ring protons in methyl sulfoxide-$\underline{d}_6$ were found to be similar to those obtained in deuterium oxide.

In a methyl sulfoxide solution, hydroxyl groups of substances associate with solvent molecules by hydrogen bonding (61). The hydroxyl groups on carbohydrates generally give their signals in the range of τ 5-6 (62). For I and its methyl ether derivatives, the chemical shifts of the hydroxyl groups (Table IV) were found in the region τ 4.8-5.4. The resonances of the hydroxyl protons are split into doublets by coupling with ring protons; therefore, spin-decoupling experiments could be used in their identification. Details of the location of the ring proton resonances are discussed later in this section (p. 37). The hydroxyl signals of the methyl ethers of I could be identified unequivocally. Only the 3- and 4-hydroxyls of 1,6-anhydro-β-D-glucopyranose (I) cannot be assigned using spin-decoupling techniques; their shifts were assigned based on the hydroxyl resonances of 1,6-anhydro-2-$\underline{O}$-methyl-β-D-glucopyranose (II). The signals of the hydroxyl hydrogens were readily eliminated from the spectrum by the addition (63, 64) of a trace of hydrogen chloride gas to the methyl sulfoxide solution.

Although the number of methoxyl groups on the methyl ethers of 1,6-anhydro-β-D-glucopyranose (I) can be readily assessed by examining the hydroxyl proton resonances, the position of substitution cannot be determined. This approach is not possible since the hydroxyl resonances of several derivatives come in the same part of the spectrum. Traces of water in the methyl sulfoxide solution, which is an extremely hygroscopic liquid, introduces another complication since the shifts of

the hydroxyl resonances move downfield with increasing amounts of water (65). For example, in the spectrum of 1,6-anhydro-β-D-glucofuranose, Fig. 25 (Appendix III), increasing the water content of the sample by 0.002% caused an equivalent decrease of 0.11 p.p.m. in the chemical shifts of all the hydroxyl peaks. The addition of traces of water does not significantly affect the resonances of the ring protons.

TABLE IV

CHEMICAL SHIFTS FOR HYDROXYL GROUPS OF 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I) AND ITS METHYL ETHERS IN METHYL SULFOXIDE-$\underline{d}_6$ WITH TMS AS INTERNAL STANDARD

1,6-Anhydroglucopyranose	Chemical Shift, τ, p.p.m.		
	OH-2	OH-3	OH-4
Levoglucosan (I)	5.32	5.12	5.20
2-O-Methyllevoglucosan (II)	--	5.01	5.22
3-O-Methyllevoglucosan (III)	5.17	--	5.07
4-O-Methyllevoglucosan (IV)	5.23	5.05	--
2,3-Di-O-methyllevoglucosan (V)	--	--	5.02
2,4-Di-O-methyllevoglucosan (VI)	--	4.88	--
3,4-Di-O-methyllevoglucosan (VII)	5.07	--	--

In the spectra of I and its seven methyl derivatives (Fig. 9-16 in Appendix III) in methyl sulfoxide-$\underline{d}_6$, the signals which appear as slightly broadened singlets at lowest field were assigned to the anomeric proton. The H-1 signal is shifted to the lowest field, i.e., the H-1 proton is being deshielded because of the electron-withdrawing effect of the two oxygen atoms on C-1 (59). The assignments of the signals for H-5, H-6' (endo), and H-6 (exo) which are only slightly affected by substitution of a methoxyl for a hydroxyl group are based on Hall's (66) and Heyns and Weyer's (59) assignments for these protons in I. The sharp singlet near τ 6.64 in the spectra of the methyl ethers of I was assigned to the methoxyl resonances.

The resonances of the remaining protons, namely H-2, H-3, and H-4, were determined by the splitting pattern of the proton's signal, or by "field-sweep" spin-decoupling experiments (67). Since the method of determining the H-2, H-3, and H-4 signals were similar for all the methyl ethers of I, a monomethyl and dimethyl derivative, 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II) and 1,6-anhydro-2,3-di-O-methyl-β-D-glucopyranose (V), will be discussed in detail to illustrate the techniques used.

The spectrum of compound (II) is given in Fig. 10 (Appendix III). The presence of the methoxyl group on the C-2 atom in compound (II) causes the signal of H-2 (τ 6.80) of 1,6-anhydro-β-D-glucopyranose (I) to move to a higher field by 0.32 p.p.m.; the H-2 signal of II resonates at τ 7.12, well apart from the unresolved signals of H-3 and H-4 (τ 6.55-6.65). This effect can be clearly seen for the H-1 signal (τ 4.80) of α-D-glucopyranose which moves to a higher field (τ_{H-1} 5.25) when the hydroxyl group on the C-1 atom is methylated to give methyl α-D-glucopyranoside (68). The doublet of narrow triplets for the H-2 signal in the spectrum of II indicates major coupling with H-3, ($J_{2,3}$ = 3.3 Hz), which was removed upon irradiation at τ 6.55 (H-3). Irradiation at H-3 also collapsed the hydroxyl doublet at τ 5.01 (OH-3) to a singlet. The chemical shift of H-4 was determined by irradiation at τ 6.65 (H-4) which collapsed the remaining hydroxyl doublet at τ 5.22 to a singlet.

In the 2,3-dimethyl ether of I, substitution of a methoxyl for hydroxyl groups again shifts the signals of H-2 and H-3 upfield as can be seen in Fig. 13 (Appendix III). The proton signals of H-2 (τ 7.06) and H-3 (τ 6.90) are clearly separated, with the H-2 signal being split into a doublet of narrow triplets due to major coupling with H-3. The signal for H-3 is split principally by H-2 and H-4 ($J_{2,3} \approx J_{2,4} \approx$ 3.0 Hz) giving a septet which collapsed to a pentet by irradiation at τ 6.60 (H-4). Irradiation at H-4 also collapsed the hydroxyl doublet (τ_{OH-4} 5.02) to a singlet.

The signal of H-6' (τ 6.25) for the dimethyl ether (V) was found to move 0.11 p.p.m. to a higher field from the H-6' signal of I on placement of a methoxyl group at the C-3 atom. This upfield shift in the H-6' signal was only observed when a methoxyl group was substituted on the C-3 atom of 1,6-anhydro-β-D-glucopyranose (I).

From the proton resonances of I and its monomethyl ether derivatives, empirical rules were obtained to account for the effects of methoxyl substitution on the chemical shifts of the ring protons in the dimethyl and trimethyl derivatives of I. The chemical shifts of I in τ values were used as reference signals with the exception of the H-3 and H-4 resonances which were not clearly resolved. These signals overlapped one another (Fig. 9, Appendix III), and their positions were determined by subtracting 0.32 p.p.m. from the chemical shift of H-3 and H-4 in 1,6-anhydro-3-O-methyl-β-D-glucopyranose (III) and 1,6-anhydro-4-O-methyl-β-D-glucopyranose (IV), respectively. For a methyl sulfoxide-d_6 solution of these 1,6-anhydrides, the rules may be formulated as follows:

1. Add 0.32 p.p.m. to the reference signal of H-2 (τ 6.80), H-3 (τ 6.62), or H-4 (τ 6.65) when a methoxyl group replaces a hydroxyl group directly on the carbon of the methine proton in question.

2a. Subtract 0.16 p.p.m. from the chemical shift of H-1 (τ 4.83) if a methoxyl group is attached to the C-2 atom.

b. Subtract 0.18 p.p.m. from the chemical shift of H-5 (τ 5.63) if a methoxyl group is attached to the C-4 atom.

c. For the remaining ring protons subtract 0.05 p.p.m. from the chemical shift of a proton bonded to the carbon atom which is adjacent to a carbon atom substituted with a methoxyl group.

3. Add 0.09 p.p.m. to the chemical shift of H-6' (τ 6.14) if a methoxyl group is attached to the C-3 atom.

Using these rules, the calculated chemical shifts of the methyl ether derivatives of I are compared in Table V with the experimentally observed values. The values are in good agreement; the largest deviation between values is 0.04 p.p.m.

Nuclear magnetic resonance spectra of the same series of 1,6-anhydrides were also obtained in deuterium oxide (Fig. 17-24 in Appendix III). The rules derived for deuterium oxide solution follow the exact format as for methyl sulfoxide, but different empirical constants must be used, and the reference signals of I also change in the new solvent. The rules are as follows:

1. Add 0.36 p.p.m. to the reference signal of H-2 (τ 6.50), H-3 (τ 6.33), or H-4 (τ 6.34) when a methoxyl group replaces a hydroxyl group directly on the carbon of the methine proton in question.

2a. Subtract 0.10 p.p.m. from the chemical shift of H-1 (τ 4.57) if a methoxyl group is attached to the C-2 atom.

b. Subtract 0.14 p.p.m. from the chemical shift of H-5 (τ 5.39) if a methoxyl group is attached to the C-4 atom.

c. For the remaining ring protons subtract 0.08 p.p.m. from the chemical shift of a proton bonded to the carbon atom which is adjacent to a carbon atom substituted with a methoxyl group.

3. Add 0.06 p.p.m. to the chemical shift of H-6' (τ 5.93) if a methoxyl group is attached to the C-3 atom.

As shown in Table VI, good agreement between the observed and calculated chemical shifts were found with the largest deviation from the predicted value being 0.03 p.p.m.

TABLE V

CHEMICAL SHIFTS FOR 1,6-ANHYDRO-β-D-GLUCOPYRANOSE AND ITS METHYL ETHERS IN METHYL SULFOXIDE-$\underline{d}_6$ WITH TMS AS INTERNAL STANDARD

1,6-Anhydro-glucopyranose[a]	Chemical Shift, τ, p.p.m.											
	H-1		H-2		H-3		H-4		H-5		H-6'	
	O[b]	C	O	C	O	C	O	C	O	C	O	C
Levoglucosan (I)	4.83	--	6.80	--	6.51-6.75	6.62	6.51-6.75	6.65	5.63	--	6.14	--
2-O-Methyl-levoglucosan (II)	4.67	4.67	7.12	7.12	6.55	6.57	6.65	6.65	5.63	5.63	6.14	6.14
3-O-Methyl-Levoglucosan (III)	4.82	4.83	6.75	6.75	6.94	6.94	6.63	6.60	5.63	5.63	6.23	6.23
4-O-Methyl-levoglucosan (IV)	4.83	4.83	6.82	6.80	6.59	6.57	6.97	6.97	5.45	5.45	6.17	6.14
2,3-Di-O-methyl-levoglucosan (V)	4.67	4.67	7.06	7.07	6.90	6.89	6.60	6.60	5.62	5.63	6.25	6.23
2,4-Di-O-methyl-levoglucosan (VI)	4.69	4.67	7.13	7.12	6.53	6.52	6.97	6.97	5.46	5.45	6.18	6.14
3,4-Di-O-methyl-levoglucosan (VII)	4.83	4.83	6.73	6.75	6.88	6.89	6.88	6.92	5.44	5.45	6.25	6.23
Trimethyl-levoglucosan (VIII)	4.66	4.67	7.04	7.07	6.88	6.84	6.88	6.92	5.42	5.45	6.25	6.23

[a] The chemical shifts of H-6 and OCH_3 for all compounds are at τ 6.48 ± 0.02 and τ 6.64 ± 0.01, respectively.

[b] O = observed and C = calculated values.

TABLE VI

CHEMICAL SHIFTS FOR 1,6-ANHYDRO-β-D-GLUCOPYRANOSE AND ITS METHYL ETHERS IN DEUTERIUM OXIDE WITH DSS AS INTERNAL STANDARD

1,6-Anhydro-glucopyranose[a]	Chemical Shift, τ, p.p.m.											
	H-1		H-2		H-3		H-4		H-5		H-6'	
	O[b]	C	O	C	O	C	O	C	O	C	O	C
Levoglucosan (I)	4.57	--	6.49	--	6.30-6.41	6.33	6.30-6.41	6.34	5.39	--	5.93	--
2-O-Methyl-levoglucosan (II)	4.47	4.47	6.85	6.85	6.18-6.40	6.25	6.18-6.40	6.34	5.40	5.39	5.93	5.93
3-O-Methyl levoglucosan (III)	4.57	4.57	6.41	6.41	6.69	6.69	6.24	6.26	5.38	5.39	5.99	5.99
4-O-Methyl-levoglucosan (IV)	4.57	4.57	6.50	6.49	6.27	6.25	6.70	6.70	5.25	5.25	5.94	5.93
2,3-Di-O-methyl-levoglucosan (V)	4.46	4.47	6.78	6.77	6.63	6.61	6.19-6.29	6.26	5.39	5.39	5.99	5.99
2,4-Di-O-methyl-levoglucosan (VI)	4.46	4.47	6.85	6.85	6.20	6.17	6.70	6.70	5.23	5.25	5.94	5.93
3,4-Di-O-methyl-levoglucosan (VII)	4.59	4.57	6.41	6.41	6.57-6.70	6.61	6.57-6.70	6.62	5.24	5.25	6.01	5.99
Trimethyl-levoglucosan (VIII)	4.46	4.47	6.78	6.77	6.48-6.65	6.53	6.48-6.65	6.62	5.23	5.25	6.01	5.99

[a] The chemical shifts of H-6 and OCH_3 for all compounds are at τ 6.29 ± 0.01 and τ 6.55 ± 0.01, respectively.

[b] O = observed and C = calculated values.

The rules for both deuterated solvents were also successfully employed in predicting the chemical shifts of several protons in 1,6-anhydro-2-O-methyl-β-D-galactopyranose (XIII) and 1,6-anhydro-4-O-methyl-β-D-mannopyranose (XIV). The results are given in Tables VII and VIII. The NMR spectra of compound XIII and XIV and the unsubstituted compounds, 1,6-anhydro-β-D-galactopyranose (XII) and 1,6-anhydro-β-D-mannopyranose (IX), are shown in Fig. 26-33 (Appendix III).

TABLE VII

CHEMICAL SHIFTS OF H-1 AND H-2 PROTONS OF 1,6-ANHYDRO-β-D-GALACTOPYRANOSE (XII) AND ITS 2-METHYL ETHER (XIII)

1,6-Anhydro-galactopyranose	Solvent	Chemical Shift, τ, p.p.m. H-1		H-2	
		O[a]	C	O	C
Levogalactosan (XII)	DMSO-d_6	4.86	--	6.51	--
	D_2O	4.59	--	6.20	--
2-O-Methyllevogalactosan (XIII)	DMSO-d_6	4.69	4.70	6.83	6.83
	D_2O	4.48	4.49	6.57	6.56

[a] O = observed and C = calculated values.

TABLE VIII

CHEMICAL SHIFTS OF H-4 AND H-5 PROTONS OF 1,6-ANHYDRO-β-D-MANNOPYRANOSE (IX) AND ITS 4-METHYL ETHER (XIV)

1,6-Anhydro-mannopyranose	Solvent	Chemical Shift, τ, p.p.m. H-4		H-5	
		O[a]	C	O	C
Levomannosan (IX)	DMSO-d_6	6.37	--	5.64	--
	D_2O	6.07	--	5.40	--
4-O-Methyllevomannosan (XIV)	DMSO-d_6	6.69	6.69	5.44	5.45
	D_2O	6.43	6.43	5.25	5.26

[a] O = observed and C = calculated values.

The self-consistency of the data on the chemical shifts of 1,6-anhydro-β-D-glucopyranose (I) and its methyl ethers indicate that the pyranose ring of these compounds exists in the 1-C (D) chair conformation. Additional evidence can be obtained concerning the ring conformation by examining the vicinal and long-range couplings of the ring protons; the magnitude of the coupling being related to the orientation of the two coupled protons (67, 69). Substitution of a methoxyl for a hydroxyl group might affect the pyranose ring conformation by either introducing steric strain, especially in the 3-methyl ether derivatives of I, or by changing the intramolecular hydrogen bonding pattern. Reeves (30) has presented evidence using a cuprammonium complexing solution, that 1,6-anhydro-β-D-glucopyranose (I) and its 3-methyl ether exist in 1-C (D) conformation.

Coupling constants, J, of the protons in compounds I-VIII were determined by first-order analysis of their spectra. For a number of signals, particularly the signals of H-6 and H-6' second-order analyses would have been more accurate; however, the weaker transitions were not detectable and consequently the spectra were not analyzable (70). Since the splitting patterns turned out to be very similar for all the derivatives, the interpretation of the spectral lines for only one 1,6-anhydride, namely 1,6-anhydro-2,3-di-O-methyl-β-D-glucopyranose (V) in methyl sulfoxide-d_6 (Fig. 13, Appendix III), will be given in detail.

The shape of the broad singlet for the signal of the anomeric proton seems characteristic of other 1,6-anhydrohexopyranoses (71-72) and results from the minor splitting of the H-1 signal by vicinal coupling with H-2 and many small magnitude splittings caused by long-range coupling of H-1 with most, if not all (67), the other ring protons. The major splitting of the H-5 into a doublet of quartets is due to coupling with H-6 ($J_{5,6}$ = 6.0 Hz) with each principal peak being further separated into four lines indicating equal coupling of small magnitude of H-5 with H-3, H-4,

and H-6' ($J_{3,5} \approx J_{4,5} \approx J_{5,6'} \approx 1.2$ Hz). Proton H-5 might also be expected to long-range couple with H-1 through the pyranose ring-oxygen, but this coupling must be weak in V as it is in 1,6-anhydro-2,3,4-tri-O-acetyl-β-D-mannopyranose ($J_{1,5} \approx 0.1$ Hz) (67).

The major splitting of the H-6' signal which appears as a quartet is due to geminal coupling with H-6 ($J_{6,6'} = 7.5$ Hz) with further small magnitude splitting by H-5 ($J_{5,6'} = 1.2$ Hz). The H-6 signal, which is partially hidden behind the methoxyl and H-4 peaks, appears as a quartet and is split as before by geminal coupling to H-6' and with further splitting by H-5.

The H-2 signal appears as a doublet of triplets with major coupling of H-2 to H-3 ($J_{2,3} = 3.3$ Hz) and additional splitting of each principal line into a triplet by equal coupling with H-1 and H-4 ($J_{1,2} \approx J_{2,4} \approx 1.2$ Hz). The H-3 signal is observed as a septet. Splitting of H-3 occurs from major coupling with H-2 ($J_{2,3} = 3.0$ Hz) and H-4 ($J_{3,4} \approx 3.0$ Hz), and from long-range coupling with H-1 and H-5 ($J_{1,3} \approx J_{3,5} \approx 1.2$ Hz).

In a similar manner, the coupling constants were determined for the remaining methyl derivatives of 1,6-anhydro-β-D-glucopyranose. The range of J values for these compounds in methyl sulfoxide-d_6 and in dueterium oxide solution are given in Table IX. The J values for each specific derivative are given in Tables XIII and XIV (Appendix IV).

The data in Table IX support a 1-C ring conformation and not a 3-B (D) conformation (30) for these 1,6-anhydrides. The small values of $J_{2,3}$ and $J_{3,4}$ (1.5-3.5 Hz) indicate the H-2, H-3, and H-4 ring protons are all equatorial; protons separated by a dihedral angle of 60° generally give coupling constants of 2-4 Hz (73), whereas protons separated by 180° (diaxially oriented) give splittings of 8-10 Hz (74). In

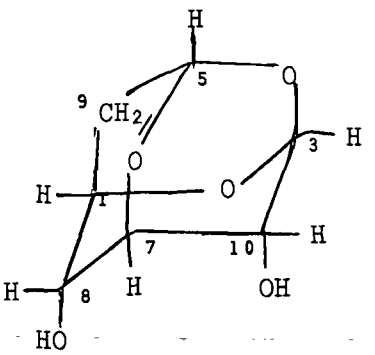
TABLE IX

RANGE OF FIRST-ORDER, COUPLING CONSTANTS FOR PROTONS OF 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I) AND ITS SEVEN METHYL ETHER DERIVATIVES

Solvent	Coupling Constant, $\underline{J}$, Hz									
	$\underline{J}_{1,2}$	$\underline{J}_{1,3}$	$\underline{J}_{2,3}$	$\underline{J}_{2,4}$	$\underline{J}_{3,4}$	$\underline{J}_{3,5}$	$\underline{J}_{4,5}$	$\underline{J}_{5,6'}$	$\underline{J}_{5,6}$	$\underline{J}_{6,6'}$
Methyl sulfoxide-$\underline{d}_6$	1.2	1.2	1.5-3.5	1.2	2.5-3.5	1.2	1.2-1.5	1.2-1.5	6.0	7.1-7.5
Deuterium oxide	1.2	1.2	2.0-3.0	1.2	3.0	1.2	1.5	1.2-1.5	6.0	7.5

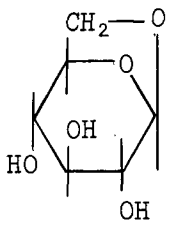
addition, the magnitudes of the long-range couplings ($^4J_{e,e}$) of H-1 with H-3, H-2 with H-4, and H-3 with H-5 indicate these pairs of protons are situated in a 1,3-diequatorial relationship, a "W-arrangement of the four bonds separating the coupled protons" (75). The value of this type of long-range coupling usually falls between 1.2-1.6 Hz (67).

Recent measurement of vicinal coupling in 8(a), 10(a)-dihydroxy-2,4,6-trioxaadamantane (XV) (75) established the order of magnitude of the coupling constants expected in the 1-C (D) chair form of 1,6-anhydro-β-D-glucopyranose (I) and its methyl ether derivatives. The coupling constants for $J_{7,8}$ and $J_{7,10}$ were 3.9 and 4.0 Hz, respectively, and $J_{1,8}$ and $J_{3,10}$ fell in the range of 1.3-1.9 Hz. These values are in the same range as the corresponding vicinal couplings (Table IX) observed for 1,6-anhydro-β-D-glucopyranose (I) and its methyl ethers.



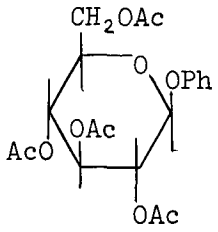
XV

GLOSSARY OF COMPOUNDS



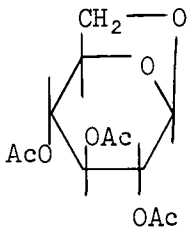
I

1,6-Anhydro-β-D-glucopyranose



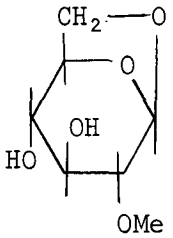
Ia

Phenyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranose



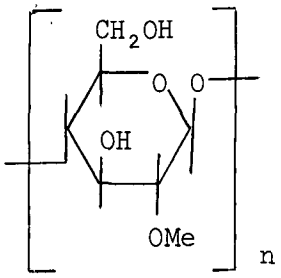
Ib

1,6-Anhydro-2,3,4-tri-O-acetyl-β-D-glucopyranose



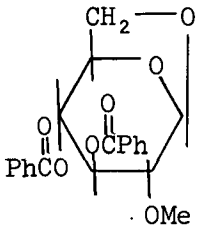
II

1,6-Anhydro-2-O-methyl-β-D-glucopyranose



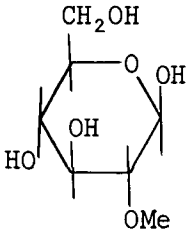
IIa

2-O-Methylcellulose



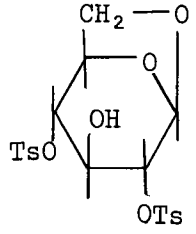
IIb

1,6-Anhydro-3,4-di-O-benzoyl-2-O-methyl-β-D-glucopyranose



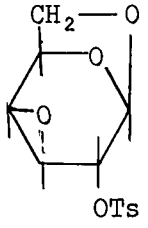
IIc

2-O-Methyl-β-D-glucopyranose



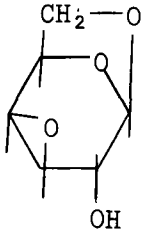
IId

1,6-Anhydro-2,4-di-O-p-toluenesulfonyl-β-D-glucopyranose



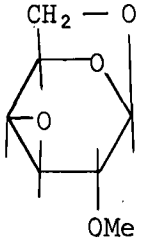
IIe

1,6:3,4-Dianhydro-2-O-p-toluenesulfonyl-β-D-galactopyranose



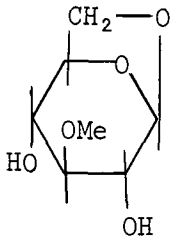
IIf

1,6:3,4-Dianhydro-β-D-galactopyranose



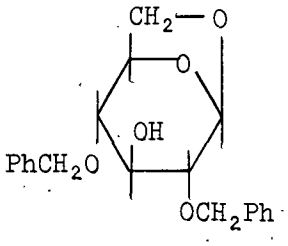
IIg

1,6:3,4-Dianhydro-2-O-methyl-β-D-galactopyranose



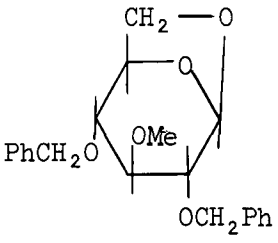
III

1,6-Anhydro-3-O-methyl-β-D-glucopyranose



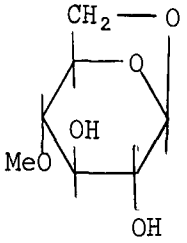
IIIa

1,6-Anhydro-2,4-di-O-benzyl-β-D-glucopyranose



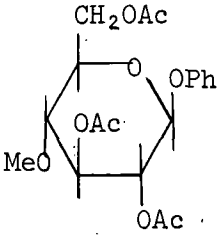
IIIb

1,6-Anhydro-2,4-di-O-benzyl-3-O-methyl-β-D-glucopyranose



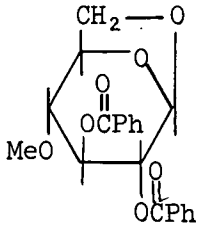
IV

1,6-Anhydro-4-O-methyl-β-D-glucopyranose



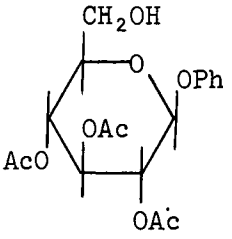
IVa

Phenyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranoside



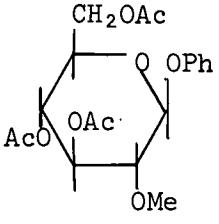
IVb

1,6-Anhydro-2,3-di-O-benzoyl-4-O-methyl-β-D-glucopyranose



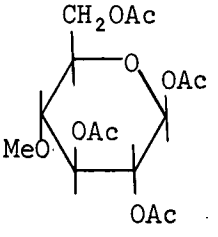
IVc

Phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside



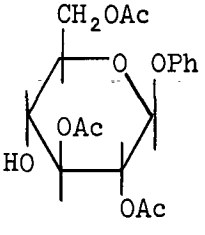
IVd

Phenyl 3,4,6-tri-O-acetyl-2-O-methyl-β-D-glucopyranoside



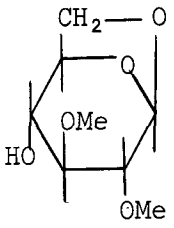
IVe

1,2,3,6-Tetra-O-acetyl-β-D-glucopyranose



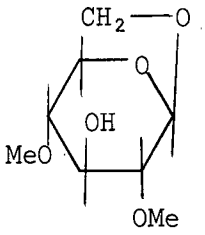
IVf

Phenyl 2,3,6-tri-O-acetyl-β-D-glucopyranoside



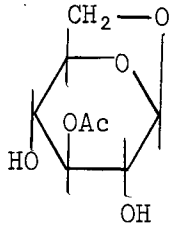
V

1,6-Anhydro-2,3-di-O-methyl
β-D-glucopyranose



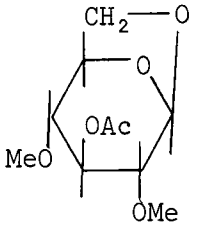
VI

1,6-Anhydro-2,4-di-O-methyl-
β-D-glucopyranose



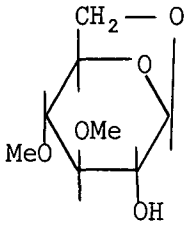
VIa

1,6-Anhydro-3-O-acetyl-
β-D-glucopyranose



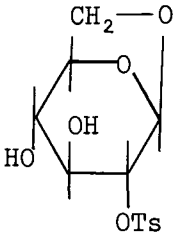
VIb

1,6-Anhydro-3-O-acetyl-2,4-di-O-
methyl-β-D-glucopyranose



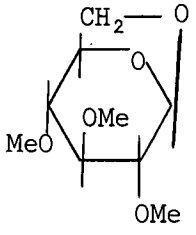
VII

1,6-Anhydro-3,4-di-O-methyl-
β-D-glucopyranose



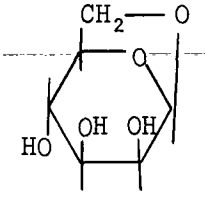
VIIa

1,6-Anhydro-2-O-p-toluenesulfonyl-
β-D-glucopyranose



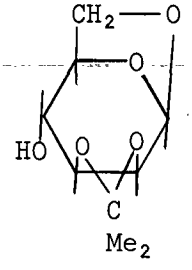
VIII

1,6-Anhydro-2,3,4-tri-O-methyl-
β-D-glucopyranose



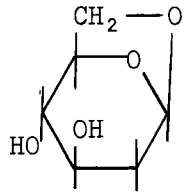
IX

1,6-Anhydro-β-D-mannopyranose



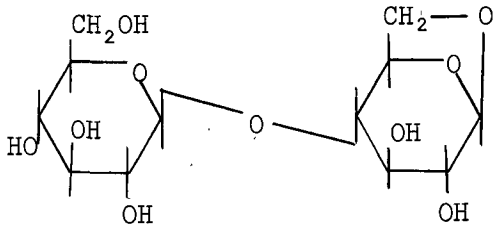
IXb

1,6-Anhydro-2,3-isopropylidene-
β-D-mannopyranose



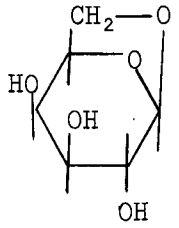
X

1,6-Anhydro-2-deoxy-β-D-
arabino-hexopyranose



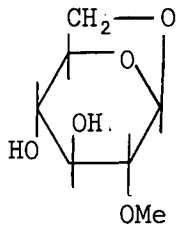
XI

1,6-Anhydro-4-O-(β-D-glucopyranosyl)-
β-D-glucopyranose



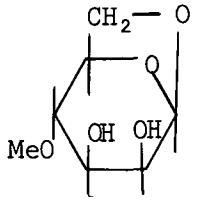
XII

1,6-Anhydro-β-D-galactopyranose



XIII

1,6-Anhydro-2-O-methyl-
β-D-galactopyranose



XIV

1,6-Anhydro-4-O-methyl-
β-D-mannopyranose

EXPERIMENTAL*

GENERAL METHODS

Melting points were determined on a Thomas Hoover Capillary Melting Point Apparatus (Arthur H. Thomas Co., Philadelphia, Pennsylvania) and were corrected.

Reactions were followed using TLC which was performed on microscope slides coated with silica gel G (Brinkmann Instruments, Inc., Great Neck, New York). Preparation of the thin-layer slides involved dipping two slides placed back to back into a rapidly stirred slurry consisting of approximately equal parts of silica gel and chloroform. The coated slides were separated, dried, sprayed with steam, and dried overnight. The plates were irrigated with a suitable developer in small weighing bottles. Common developers employed were (a) a mixture of ethyl acetate and methanol (2:1) for polar compounds, and (b) ethyl acetate for nonpolar compounds. Visualization of the components on the plate was accomplished by spraying the plate with a 10% solution of sulfuric acid in methanol and charring on a hot plate.

Anhydrous ethanol was obtained by the general procedure of Fieser (76). Anhydrous pyridine was prepared as described by Fieser (77) and after distillation was stored over calcium hydride until used. N,N-Dimethylformamide was dried over calcium hydride (78). p-Dioxane was purified according to the procedure of Fieser (79). Anhydrous acetone was prepared by refluxing commercial acetone with Drierite for several hours followed by distillation. Ethyl acetate was distilled prior to use.

*See Glossary of Compounds, p. 47.

Silver oxide was prepared by the procedure of Angyal and Melrose (80). Hydroxylamine was obtained by reacting sodium butylate and hydroxylamine hydrochloride according to the method of Hurd and Brownstein (81).

Solutions were evaporated *in vacuo* (≈ 22 mm. Hg) below 50°.

The disappearance of monomer in the polymerization reactions was followed quantitatively by trimethylsilylation and measurement by GLC. All analyses were performed on an Aerograph Hy-Fi gas chromatograph (Model A-600-B, Varian Aerograph, Walnut Creek, California) equipped with a hydrogen flame ionization detector. The column (5-foot length) was an 1/8-inch stainless steel tube containing 5% w/w SE-30 on 60/80 mesh chromosorb W (Varian Aerograph). The column was operated isothermally at 170-3° for all 1,6-anhydrides except compound (X) where the temperature was 164-7°. The injection chamber temperature was 250°. Dry nitrogen was used as the carrier gas at a pressure of 10-12 lb. The hydrogen flow to the detector flame was approximately 30 ml./min. Because the retention time (> 1 hr.) of the disaccharide, XI, was long, the gas chromatograph was operated at a column temperature of 260-5° and an injector temperature of 325°. The nitrogen and hydrogen flow rates were the same as for the other 1,6-anhydrides.

Nuclear magnetic resonance spectra were recorded at probe temperature, 40°, on a Varian A-60A Analytical NMR Spectrometer. Chemical shifts are given in τ values (p.p.m.) from the reference signal of either tetramethylsilane (TMS) in methyl sulfoxide-d_6 (99.5% D, Stohler Isotope Chemicals, Rutherford, New Jersey) and chloroform-d (99.8% D, 1% v/v TMS, Stohler) or of sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS) in deuterium oxide (99.8% D, Stohler). For each spectrum, approximately 30-50 mg. of compound was dissolved in 0.4-0.5 ml. of deuterated solvent and for a spectrum in deuterium oxide approximately 5 mg. of DSS were added. For spectra obtained in deuterium oxide, proton resonances which were hidden behind the HOD peak at 40° were

made visible by heating the sample to approximately 80° which shifted the HOD peak upfield (82). Spin-decoupling experiments were performed using the "field-sweep" method (67).

The shifts which were read directly from a spectrum are estimated to be accurate to ± 1 Hz (± 0.02 p.p.m.). This estimate is based on the signal of methyl sulfoxide-d_5 (τ 7.48) which is an isotopic contaminant in methyl sulfoxide-d_6. The shifts of the proton resonances which were located by spin-coupling experiments are estimated to be accurate to ± 2 Hz (± 0.03 p.p.m.).

PREPARATION OF COMPOUNDS

1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I)

The procedure of Coleman (17) was used to prepare I; m.p. 179° $[\alpha]_D^{25}$ -66.0° (c 3.40, water); lit. (83), m.p. 179-180°, $[\alpha]_D$ -66.2° (c 2.0, water).

2-O-Methylcellulose (IIa) was prepared by a slight modification of the procedure of Falconer and Purves (18).

2,3,6-TRI-O-NITROCELLULOSE

The procedure of Bennett and Timell (84) was modified to prepare 2,3,6-tri-O-nitrocellulose. In a dry ice-acetone bath, 90% nitric acid (340 ml.) was cooled to -40° and decolorized by passing a slow stream of dry nitrogen through the solution for 15 min. Acetic anhydride (500 ml.) which had been cooled to -20° was added slowly to the decolorized nitric acid solution with the temperature of the mixture being kept below -20°. The nitrating mixture was added over a period of 2 min. to 5.37 g. of dried acetate-grade cotton linters in a 1-liter reaction flask cooled to -20° in a dry ice-acetone bath. The reaction flask was placed in an ice-bath and the mixture was stirred occasionally. After 3 hr., the reaction mixture was filtered in a coarse,

sintered-glass funnel, and the funnel and its contents quickly transferred to another suction flask where the 2,3,6-tri-O-nitrocellulose was washed with water at 4° (8 liters) and with methanol (1 liter). The product was stabilized by suspension in methanol (300 ml.) overnight at 0° and was removed by filtration and air dried; yield 9.60 g. (99.4%). Three additional 5-6 g. batches of cellulose were nitrated to give a total of 38.3 g. of 2,3,6-tri-O-nitrocellulose. Two to three-gram samples of product were stored over phosphorous pentoxide in a desiccator with care taken to avoid grinding fragments of the dangerous explosive under the glass lid of the container.

Anal. Found: N (Kjeldahl), 14.0, 14.1%; based on nitrogen content, D.S. NO_3, 2.97.

3,6-di-O-NITROCELLULOSE

The procedure of Segall and Purves (85) was modified to synthesize 3,6-di-O-nitrocellulose. Freshly prepared hydroxylamine (64.5 g.) (61) was dissolved in anhydrous pyridine (300 ml.) at 4° and the solution added to the compound, 2,3,6-tri-O-nitrocellulose (18.7 g.). On warming to room temperature, the reaction mixture became a viscous, amber-colored solution which swelled with the evolution of nitrogen. When the production of nitrogen slackened, the mixture was placed in the dark for 3 days, after which the solution, now at a somewhat lower viscosity, was poured with stirring into water (2 liters). The white fibrous precipitate was collected on a coarse, sintered-glass funnel, washed with additional water (2 liters), and air dried. The fibrous product was dissolved in a mixture of p-dioxane and acetone (600 ml., 1:1) and precipitated by pouring the solution into water (3 liters) with rapid stirring to keep the fibrous precipitate in suspension. The product was removed by filtration, air dried, and then dried *in vacuo* over phosphorous pentoxide to give 14.4 g. (93.6%) of 3,6-di-O-nitrocellulose. The denitration procedure was repeated on an additional

17.3 g. of 2,3,6-tri-O-nitrocellulose to give a total yield of 29.0 g. of 3,6-di-O-nitrocellulose.

Anal. Found: N (Kjeldahl) 10.0, 10.2%; based on nitrogen content, D.S. NO_3 1.73. Lit. (85): N, 10.60, 10.52%.

2-O-METHYL-3,6-DI-O-NITROCELLULOSE

Segall and Purves' (85) procedure was modified to prepare 2-O-methyl-3,6-di-O-nitrocellulose. 3,6-Di-O-nitrocellulose (26.3 g.) was dissolved in freshly distilled p-dioxane (1.6 liters) and was methylated in a nitrogen atmosphere at room temperature by the slow, simultaneous addition of 16.7M aqueous sodium hydroxide solution (127 ml.) and dimethyl sulfate (168 ml.) over a period of 6 hr. After 24 hr. at room temperature, the amber-colored reaction mixture was placed in ten cellophane bags (44 x 200 mm.) and dialyzed in running tap water until neutral to pH paper ($\approx$ 2 hr.). The dialytic bags were placed in distilled water overnight after which the nondialyzable material was lyophilized to yield 21.9 g. (84.7%) of 2-O-methyl-3,6-di-O-nitrocellulose.

Anal. Found: N (Kjeldahl), 7.57, 7.65%; OCH_3, 13.64, 13.80%; based on nitrogen and methoxyl contents, D.S. NO_3, 1.27 and D.S. OCH_3, 1.04. Lit. (85): N, 9.5%; OCH_3, 12.3%.

2-O-METHYLCELLULOSE (IIa)

The procedure of Falconer and Purves (18) was modified to prepare IIa. In a 1-liter, three-necked flask equipped with a mechanical stirrer, 2-O-methyl-3,6-di-O-nitrocellulose (21.6 g.) was dissolved in freshly prepared p-dioxane (175 ml.); solution being complete in approximately 3 hr. To this solution at room temperature was added slowly a 39% aqueous ammonium hydrosulfide solution (375 ml.) (18) which

resulted in a highly swollen gel that redissolved after stirring the mixture for 24 hr. The orange-colored reaction mixture was diluted with water (200 ml.) and allowed to remain at room temperature for an additional 36 hr. The mixture, with several milliliters of n-butanol added to reduce foaming, was then concentrated to remove most of the ammonium hydrosulfide. The product was precipitated with absolute ethanol (250 ml.), recovered by centrifugation, and washed twice with absolute ethanol (200 ml.). The ethanolic liquors were combined, evaporated to approximately 50 ml., and upon dilution with acetone precipitation of a second fraction of product occurred. The fractions were combined and extracted for 48 hr. in a Soxhlet extractor with a mixture of acetone and carbon disulfide (3:4). The orange-colored gel was washed three times with hexane and dried to give 10.1 g. (60.4%). The methylated material was dissolved in water and lyophilized to give a yellow-colored IIa.

Anal. Found: N (Kjeldahl), 0.96, 1.00%; OCH_3, 16.04, 16.20%; S, 1.89%; based on nitrogen and methoxyl contents, and with sulfur present in elemental form, D.S. NO_3, 0.13 and D.S. OCH_3, 0.94. Lit. (18): N, 1.08, 1.06%; OCH_3, 19.0, 18.8%.

1,6-ANHYDRO-3,4-DI-O-BENZOYL-2-O-METHYL-β-D-GLUCOPYRANOSE (IIb); PYROLYSIS OF 2-O-METHYLCELLULOSE (IIa)

Pyrolysis of 2-O-methylcellulose (IIa) was performed on 0.5-g. charges in a pyrex test tube (20 x 140 mm.) fitted with a 19/38 female, ground-glass joint. A plug of glass wool was placed directly over the charge, and the test tube fitted with a copper cooling coil positioned externally about 50 mm. from the charge. The test tube was positioned horizontally, and after evacuation to 0.02 mm. Hg, the end of the tube was inserted into a combustion furnace (Model 2A, Hoskins Mfg. Co., Detroit, Michigan) held at a constant temperature of 350°. Distillate began collecting immediately on the cooled portion of the tube, and heating was continued for 1 hr. The distillate was dissolved in water, the solution passed through Amberlite MB-3 (H^+, OH^-) resin, and the effluent from the column evaporated to give 0.27 g. (57%)

of an amber-colored viscous sirup. The deionized distillates from ten separate pyrolyses were combined to give 2.88 g. of sirup which was dissolved in anhydrous pyridine (30 ml.). This solution was cooled to 4° and benzoyl chloride (9 ml.) added in 1-ml. portions at 5-min. intervals. The reaction mixture was kept at 4° for 24 hr. and allowed to stand an additional 5 hr. at room temperature. Water (1 ml.) was added to destroy excess benzoyl chloride, and after 1 hr. at room temperature, 1,2-dichloroethane (75 ml.) was added to the reaction mixture. The organic phase of the reaction mixture was washed successively with cold 1.5M aqueous sulfuric acid, aqueous sodium hydrogen carbonate, and water. The 1,2-dichloroethane solution was dried over sodium sulfate and evaporated to a sirup. The product crystallized from a mixture of chloroform and methanol to give 3.89 g. (62%, based on benzoylation procedure) of material m.p. 140-5°. Recrystallization from methanol gave pure IIb, m.p. 145.5-6.5°, $[\alpha]_D^{25}$ -192° (c 1.14, chloroform).

Anal. Calc. for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.79; H, 5.29.

1,6:3,4-DIANHYDRO-2-O-p-TOLUENESULFONYL-β-D-GALACTOPYRANOSE (IIe)

The method of Carlson (19) was employed to prepare IIe, m.p. 148-9°, $[\alpha]_D^{26}$ -40.3° (c 2.18, chloroform); lit. (19), m.p. 150-1°, $[\alpha]_D^{28}$ -37° (c 1.5, chloroform).

1,6:3,4-DIANHYDRO-β-D-GALACTOPYRANOSE (IIf)

The procedure of Hook and Lindberg (20) was used to synthesize IIf, m.p. 68-7°, $[\alpha]_D^{25}$ -73.9° (c 2.34, water); lit. (20), m.p. 69-71°, $[\alpha]_D^{21}$ -81° (c 1.0, water).

1,6:3,4-DIANHYDRO-2-O-METHYL-β-D-GALACTOPYRANOSE (IIg)

A Purdie methylation of 1,6:3,4-dianhydro-β-D-galactopyranose (IIf) as performed by Cerny, Buben, and Pacak (21) was used to prepare IIg, m.p. 91-2°, $[\alpha]_D^{28}$ -73.6° (c 2.24, chloroform); lit. (21), m.p. 91.3°, $[\alpha]_D^{20}$ -77° (c 1.35, chloroform).

1,6-ANHYDRO-2-O-METHYL-β-D-GLUCOPYRANOSE (II)

a) 1,6-Anhydro-3,4-di-O-benzoyl-2-O-methyl-β-D-glucopyranose (IIb), (3.82 g.), was dissolved in chloroform (40 ml.) to which was added anhydrous methanol (40 ml.). To this solution was added a solution of sodium (0.2 g.) dissolved in methanol (10 ml.) and after 1 hr. at room temperature, the reaction mixture was diluted with 75 ml. of water. The chloroform phase was extracted three times with distilled water, the combined aqueous phases were passed through an Amberlite MB-3 (H^+, OH^-) resin, and the effluent concentrated to a sirup (2.06 g.). A small portion of the sirup was distilled under reduced pressure at 1 mm. using a microsublimation apparatus to give a distillate that crystallized. A solution of the sirup in a mixture of acetone and hexane was seeded and set in the cold (-10°). The crop of crystals, 1.65 g. (94.3%), m.p. 92-4°, was recrystallized twice from acetone-hexane to give pure II, m.p. 93-4°, $[\alpha]_D^{25}$ -72.7° (c 1.45, acetone).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.73; H, 6.87. Found: C, 47.93; H, 6.69.

b) 1,6:3,4-Dianhydro-2-O-methyl-β-D-galactopyranose (IIg) (0.309 g.), was refluxed 14 hr. in 1M aqueous potassium hydroxide solution (25 ml.); at which time TLC (developer ethyl acetate) showed complete consumption of starting material. The reaction mixture was diluted with water (20 ml.), neutralized by passage through Amberlite MB-3 (H^+, OH^-) resin, and concentrated to give a colorless sirup. The sirup was crystallized as before from acetone-hexane to give 0.243 g. (70.5%) of material with m.p. 84-7°. Two recrystallizations from ethyl acetate gave a material whose NMR, specific optical rotation, melting and mixed melting points were identical to those of II prepared in part (a).

ACID-HYDROLYSIS OF 1,6-ANHYDRO-2-O-METHYL-β-D-GLUCOPYRANOSE (II)

1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II), (0.19 g.), was refluxed 72 hr. in 0.075M sulfuric acid (30 ml.). The solution was cooled, neutralized by passage through Amberlite MB-3 (H^+, OH^-) resin, and concentrated to give 0.11 g. (52%) of sirup. The product was crystallized in absolute ethanol at -10° after seeding to give 0.056 g. (27%) of material, m.p. 155.5-6.5°. A mixed melting point with 2-O-methyl-β-D-glucopyranose (IIc) (155-7°) (86), which was crystallized from an absolute ethanol solution according to the method of Falconer and Purves (18), was essentially undepressed, m.p. 153-6°. The NMR spectra of the samples in deuterium oxide were identical. NMR data: τ 4.58 (doublet, H-1_α), τ 5.37 (doublet, H-1_β); τ 6.15-6.33 (multiplet); τ 6.41, 6.53 (singlets, methoxyl); and τ 6.43-6.75 (multiplet).

PARTIAL METHYLATION OF 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I)

In a 1-liter, two-necked flask equipped with a mechanical stirrer was dissolved 10.1 g. (0.06 mole) of 1,6-anhydro-β-D-glucopyranose (I) in methyl sulfoxide (200 ml.). To this solution at room temperature was added with stirring sodium hydroxide pellets (60.0 g.) followed by the slow addition of a mixture of methyl sulfate (5.8 ml., 0.06 mole) in methyl sulfoxide (100 ml.) over a period of 12 hr. Stirring of the reaction mixture continued for an additional 12 hr., after which the viscous, amber-colored mixture was diluted with 500 ml. of water to dissolve the solids, and the solution heated on a steam bath for 1 hr. to destroy the excess methyl sulfate. The solution was cooled to room temperature, neutralized with 1M aqueous sulfuric acid solution, concentrated at 1 mm. Hg, and absolute ethanol (100 ml.) was added to the residue. The solution was filtered to remove sodium sulfate, and the filtrate was concentrated to a sirup (24.9 g.) which contained a large amount of methyl sulfoxide. A portion of the sirupy methyl sulfoxide solution (15.5 g.) was fractionated by column chromatography on 500 g. of silica gel (Davison, Grade 950, mesh 60-200) where the

ratio of column diameter to length was 1 to 17. The column was first washed with 12 liters of chloroform to remove the methyl sulfoxide and then washed with ethyl acetate. Ten-milliliter fractions of effluent were collected automatically. Fractions 80 to 95 were combined, and the ethyl acetate was evaporated to give a sirup (0.36 g.) which was shown to contain only the monomethyl ethers of I by TLC (developer ethyl acetate). The sirup showed only one spot (R_f 0.34), which had the same mobility as II. Using the same developer, the dimethyl and trimethyl ethers of I have R_f of 0.45 and 0.61, respectively. The sirup was acetylated in a mixture of anhydrous sodium acetate (1.5 g.) and acetic anhydride (6 ml.) which was heated to boiling over a flame. The reaction mixture was permitted to cool to room temperature, poured with stirring into ice water, and stirred for 3 hr. The aqueous solution was extracted with chloroform and the chloroform solution washed with saturated, aqueous sodium hydrogen carbonate and water. After drying the chloroform solution over sodium sulfate, the mixture was treated with activated charcoal, filtered through Celite, and the chloroform evaporated to give a colorless sirup (0.30 g.). Attempts to crystallize the sirup from 95% ethanol at 0° failed. The acetylated product was deesterified in the usual manner with 1% sodium methoxide in methanol. The resulting sirup was dissolved in deuterium oxide, and using the NMR method described in the following section, it was determined that the monomethyl fraction contained 54, 10, and 36% of the 2-, 3-, and 4-methyl ethers of I.

NMR METHOD OF ANALYSIS OF A MIXTURE OF MONOMETHYL 1,6-ANHYDRO-β-D-GLUCOPYRANOSES (II, III, IV)

Nuclear magnetic resonance was employed to determine the composition of a mixture of the monomethyl ethers of I. The method is possible because of the unique chemical shifts of certain protons on the individual ether derivatives.

The H-1 resonance of the 2-methyl ether is shifted slightly to a lower field than the H-1 resonances of the 3- and 4-methyl ethers of I, Table VI. From the integrated intensities of the different H-1 signals, the weight percent of II can be determined. The weight percent of II may also be derived from the signals of the methine protons of the carbon atom bearing the methoxyl groups. The H-2 resonance of the 2-methyl ether (II) occurs at a higher field than the H-3 and H-4 signals of the 3- and 4-methyl ethers (III and IV).

The weight percent of III is based on the relative areas of the H-6' signals. The H-6' signal is shifted upfield by 0.06 p.p.m. from the signal of the H-6' in both the 2- and 4-methyl ethers. The quantity of IV is calculated by difference.

The NMR spectrum of a mixture of known composition of the monomethyl ethers in deuterium oxide is shown in Fig. 34 (Appendix III). The weight percent of each monomethyl ether was determined as described above (Table X). At the composition chosen, the relative precision between observed and calculated is approximately $\pm$ 3%.

The spectrum of the monomethyl fraction, obtained as described in the preceding section, by the methylation of I is shown in Fig. 35 (Appendix III). As seen in Fig. 35, the signal of the H-6' of the 3-methyl ether of I is small compared with the combined H-6' signals of the 2- and 4-methyl ethers. The estimate of the composition of the monomethyl fraction is given in Table X.

1,6-ANHYDRO-2,4-DI-O-BENZYL-β-D-GLUCOPYRANOSE (IIIa)

The procedure of McCloskey (28) was modified to prepare IIIa. 2,3,4-Tri-O-acetyl-1,6-anhydro-β-D-glucopyranose (Ib) (61.7 g.), xylene (200 ml.), and benzyl chloride (250 ml.) were placed in a 1-liter, three-necked flask equipped with a mechanical stirrer and a reflux condenser. The flask was initially warmed to 90° in an oil bath and powdered potassium hydroxide (100 g.) added slowly with vigorous

TABLE X

NMR ANALYSIS OF MONOMETHYLATED 1,6-ANHYDRO-β-D-GLUCOPYRANOSES IN DEUTERIUM OXIDE WITH DSS AS INTERNAL STANDARD

	Known Composition		Unknown Composition
1,6-Anhydroglucopyranose	Observed % wt. 1,6-Anhydro Sugar	Calculated % wt. 1,6-Anhydro Sugar	Observed % wt. 1,6-Anhydro Sugar
2-O-Methyllevoglucosan	36.2[a], 31.7[b]	33.3	53.6[a], 53.5[b]
3-O-Methyllevoglucosan	36.1[c]	32.6	10.4[c]
4-O-Methyllevoglucosan	29.9[d]	34.1	36.0[d], 36.1[d]
		100.0	

[a]Based on H-1 signals.
[b]Based on H-2, H-3, and H-4 signals of only those carbon atoms bearing methoxyl groups.
[c]Based on H-6' signals.
[d]Determined by difference from 100%.

stirring over a period of 30 min. The temperature of the reaction mixture during this time period rose to approximately 120°. Stirring was continued for another 30 min., the mixture cooled to room temperature, and diluted with water (400 ml.). The aqueous layer was separated, extracted with benzene (40 ml.), the benzene extract combined with the nonaqueous layer, and the combined solution extracted with water (50 ml.). The organic solution was transferred to a Claisen flask and benzyl chloride and benzyl alcohol were removed by distillation at 100°/1 mm. Hg. The residue was dissolved in 95% ethanol to which water (10 ml.) was then added, and the solution was set aside to crystallize overnight at room temperature. After removal of the crystalline 1,6-anhydro-2,3,4-tri-O-benzyl-β-D-glucopyranose (47.7 g., 51.2%) by filtration, the filtrate was concentrated and the residue dissolved in 95% ethanol (100 ml.). Crystallization occurred upon seeding with 1,6-anhydro-

2,4-di-O-benzoyl-β-D-glucopyranose to give 19.6 g. (26.5%) of product, m.p. 81-4°. Recrystallization from 95% ethanol and drying in an Abderhalden apparatus for 48 hours at 56°/1 mm. Hg to remove remaining traces of benzyl alcohol gave pure IIIa, m.p. 102-3°; lit. (28), m.p. 103°.

1,6-ANHYDRO-3-O-METHYL-β-D-GLUCOPYRANOSE (III)

The procedure of Reeves (30) was modified to synthesize III. To a solution of 1,6-anhydro-2,4-di-O-benzyl-β-D-glucopyranose (IIIa) (5.09 g.) in anhydrous methanol was added, with stirring, silver oxide (20 g.), powdered anhydrous calcium sulfate (2 g.), and methyl iodide (25 ml.). The mixture was refluxed for 8 hr., the calcium and silver salts filtered off, and the filtrate concentrated to a sirup. The methylation was repeated to give 5.53 g. of sirupy product. Debenzylation of the sirupy 1,6-anhydro-2,4-di-O-benzyl-3-O-methyl-β-D-glucopyranose (IIIb) was accomplished by dissolving the sirup (5.53 g.) in ethyl acetate to which was added 2 g. of palladium-on-charcoal (10% palladium), and placing the mixture in a Parr hydrogenator at 40 atm. of hydrogen for 24 hr. at room temperature. The catalyst was removed by filtration, the filtrate concentrated, and the resulting sirup was hydrogenated once more as above. Crystallization of the resulting sirup occurred from a mixture of acetone and isopropyl ether at -10° after seeding to give 1.37 g. (52.3%) of product, m.p. 65-7°. Seed crystals were obtained by distilling a small portion of sirupy product using a microsublimator. The product was recrystallized twice from acetone-isopropyl ether to give pure III; m.p. 65-7°, $[\alpha]_D^{30}$ -59.0° (c 1.00, acetone); lit. (30), m.p. 63-4°, $[\alpha]_D^{25}$ -64.5° (c 0.52, acetone).

1,2,3,6-TETRA-O-ACETYL-4-O-METHYL-β-D-GLUCOPYRANOSE (IVe)

The procedure described by Mastronardi, et al. (31) was employed to synthesize IVe, m.p. 104-5°, $[\alpha]_D^{25}$ -13° (c 3.40, chloroform); lit. (31), m.p. 103-4°, $[\alpha]_D^{20}$ -10.2° (c 1.1, chloroform).

PHENYL 2,3,4-TRI-O-ACETYL-β-D-GLUCOPYRANOSIDE (IVc)

The method as described by Seib (38) was used to prepare IVc, m.p. 139-41°, $[\alpha]_D^{25}$ -17° (c 2.78, chloroform); lit. (38), m.p. 137-8°, $[\alpha]_D^{25}$ -19° (c 2.1, chloroform).

PHENYL 2,3,6-TRI-O-ACETYL-β-D-GLUCOPYRANOSIDE (IVf)

The procedure of Helferich and Strauss (32) was modified to prepare IVf. To a solution of phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (IVc), (2.52 g.), in 35 ml. of 95% ethanol was added 0.1M aqueous sodium hydroxide (28 ml.). The reaction mixture was held at room temperature for 5 min. and was then neutralized by the addition of 1M aqueous acetic acid (3.0 ml.). Evaporation of the reaction mixture to dryness left a residue which was extracted three times with chloroform. The chloroform solution was concentrated to a sirup which crystallized from 95% ethanol to give 1.63 g. (64.7%) of material, m.p. 129-34°. After recrystallization from 95% ethanol, pure IVf was obtained, m.p. 137-8°, $[\alpha]_D^{24}$ -52.9° (c 2.74 chloroform); lit. (32), m.p. 130°, $[\alpha]_D^{18}$ -52.2° (c 3.98, chloroform). When IVc and IVf were mixed, the melting point was depressed.

PHENYL 2,3,6-TRI-O-ACETYL-4-O-METHYL-β-D-GLUCOPYRANOSIDE (IVa)

a) To a warm solution of phenol (2.0 g.) and p-toluenesulfonic acid (0.03 g.) (87) was added 1,2,3,6-tetra-O-acetyl-4-O-methyl-β-D-glucopyranose (IVe), (1.15 g.). The reaction mixture was heated on a steam bath for 1 hr. under diminished pressure (∿ 15 mm.), and after cooling to room temperature, the red-colored reaction mixture was dissolved in benzene (20 ml.). The benzene solution was washed four times with 1M aqueous sodium hydroxide, three times with water, and dried over sodium sulfate. Evaporation of the benzene gave a sirup that crystallized at -10° from 95% ethanol to give 0.810 g. (50.8%) of material. Recrystallization from 95% ethanol gave pure

IVa, m.p. 87-9°, $[\alpha]_D^{24}$ -39.9° (c 3.03, chloroform): NMR data (chloroform-d); τ 2.53-3.17 (5 protons, multiplet, phenyl); τ 4.66-5.03 (3 protons, multiplet); τ 5.50-5.75 (2 protons, multiplet); τ 6.10-6.53 (2 protons, multiplet); τ 6.55 (3 protons, singlet, methoxyl); τ 6.25, 6.29, 6.32 (9 protons, singlets, acetyl).

Anal. Calc. for $C_{19}H_{24}O_9$: C, 57.57; H, 6.10. Found: C, 57.41; H, 6.05

b) In order to confirm the structure assigned to phenyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranoside (IVa), the compound phenyl 2,3,6-tri-O-acetyl-β-D-glucopyranoside (IVf) was methylated under conditions described by Mastronardi, et al. (31), wherein acetyl migration does not occur. Phenyl 2,3,6-tri-O-acetyl-β-D-glucopyranoside (IVf), (1.15 g.), was dissolved in dichloromethane (20 ml.) (88), the solution cooled to 0°, and boron trifluoride etherate (0.04 ml.) was added. To this solution at 0° was added slowly with stirring a solution of diazomethane in dichloromethane previously dried over potassium hydroxide pellets. Addition was stopped after a faint yellow color remained in the reaction mixture for a short period of time. The reaction mixture was permitted to stand at 0° for 30 min. after which the precipitated polymethylene was removed by filtration. The filtrate was successively washed with aqueous sodium hydrogen carbonate and with water, and dried over sodium sulfate. Evaporation of the dichloromethane gave a sirup which crystallized from 95% ethanol to yield 0.770 g. (64.5%) of product. Recrystallization from 95% ethanol gave IVa, m.p. 87-9°, and a mixed-melting point with the material prepared as described in part (a) was undepressed.

c) The following procedure was used to prepare IVa in quantity. Phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (IVc), (19.8 g.), methyl iodide (50 ml.), and anhydrous N,N-dimethylformamide (200 ml.) were stirred together, the mixture was cooled to 4°, and freshly prepared silver oxide (60 g.) added in six portions over a period of 1-1/2 hr. Stirring was continued for 4-1/2 hr. at 4°. The silver salts

were removed by filtration and washed with a small portion of N,N-dimethylformamide. Chloroform (200 ml.) was added to the filtrate, and the chloroform solution was washed three times with 6% aqueous potassium cyanide. The combined potassium cyanide washings were extracted twice with chloroform (120 ml.). The combined chloroform phases were washed twice with water (200 ml.) and dried over sodium sulfate. Evaporation of the chloroform gave a sirup which crystallized from 95% ethanol to give 11.5 g. (56.2%) of material, m.p. 85-9°. Recrystallization from 95% ethanol yielded pure IVa, m.p. 87-9°. A mixed-melting point between this compound and the material in part (a) was undepressed.

1,6-ANHYDRO-4-O-METHYL-β-D-GLUCOPYRANOSE (IV)

Phenyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranoside (IVa), (5.10 g.), was dissolved in 2-methoxyethanol (40 ml.) and to this solution was added 2M aqueous potassium hydroxide (100 ml.). Upon mixing these solutions, a white precipitate formed that redissolved upon shaking. The mixture was refluxed for 48 hr. after which the amber-colored solution was cooled to room temperature, diluted with distilled water (200 ml.), and deionized by passage through Amberlite MB-3 (H^+, OH^-) resin. Evaporation of the effluent gave a colorless sirup (2.54 g.), which crystallized from a mixture of acetone and hexane at -10° after seeding to give 1.39 g. (61.2%) of material. Seed crystals were obtained by molecular distillation using a microsublimator. Two recrystallizations of IV from acetone-hexane gave pure material, m.p. 67-8°, $[\alpha]_D^{25}$ -65.4° (c 3.21, acetone).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.73; H, 6.87. Found: C, 47.97; H, 6.88.

1,6-ANHYDRO-2,3-DI-O-BENZOYL-4-O-METHYL-β-D-GLUCOPYRANOSE (IVb)

To a solution at 4° of 1,6-anhydro-4-O-methyl-β-D-glucopyranose (IV), (0.105 g.), in anhydrous pyridine was added benzoyl chloride (0.25 ml.) in two portions

over a period of 10 min. The reaction mixture was kept at 0° overnight. The excess benzoyl chloride in the mixture was then destroyed by the addition of water (0.5 ml.), and after 1 hr. at room temperature, 1,2-dichloroethane (50 ml.) was added to the reaction mixture. The organic phase was separated and washed successively with aqueous 1.5M aqueous sulfuric acid, aqueous sodium hydrogen carbonate, water, and dried over sodium sulfate. Concentration of the 1,2-dichloroethane solution gave a sirup which crystallized from methanol to give 0.086 g. (38%) of material, m.p. 110-11.5°. Recrystallization from methanol gave pure IVb, m.p. 110-11.5°, $[\alpha]_D^{26}$ +91.9° (c 1.51, chloroform).

Anal. Calc. for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.60; H, 5.33.

PHENYL 3,4,6-TRI-O-ACETYL-2-O-METHYL-β-D-GLUCOPYRANOSIDE (IVd)

Concentration of the mother liquor from the preparation of phenyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranoside (IVa) by treatment of phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (IVc) with methyl iodide and silver oxide in N,N-dimethylformamide yielded a second crop of crystalline product weighing 5.95 g. (29.0%), m.p. 77-88°. Three recrystallizations from methanol gave phenyl 3,4,6-tri-O-acetyl-2-O-methyl-β-D-glucopyranoside (IVd), m.p. 110-12°, $[\alpha]_D^{2.5}$ -21° (c 1.78, chloroform): NMR data (chloroform-d); τ 2.53-3.13 (5 protons, multiplet, phenyl); τ 4.64-5.14 (3 protons, multiplet); τ 5.70-5.86 (2 protons, multiplet); τ 5.96-6.40, 6.42-6.70 (2 protons, multiplet); τ 6.41 (3 protons, singlet, methoxyl); τ 6.27, 6.30, 6.33 (9 protons, singlets, acetyl).

Anal. Calc. for $C_{19}H_{24}O_9$: C, 57.57; H, 6.10. Found: C, 57.98; H, 6.16.

The position of the methoxyl group in this glucoside (IVd) was determined as follows: Phenyl 3,4,6-tri-O-acetyl-2-O-methyl-β-D-glucopyranoside (IVd), (0.499 g.), was dissolved in anhydrous methanol (5 ml.) to which was added approximately 0.002 g.

of sodium in 1 ml. of anhydrous methanol. After 30 min. at room temperature, the reaction mixture was diluted with water (10 ml.) and deionized by passage through Amberlite MB-3 (H^+, OH^-) resin. Evaporation of the effluent yielded a crystalline residue that was recrystallized from hot water to give 0.118 g. of phenyl 2-O-methyl-β-D-glucopyranoside, m.p. 168-9°. A second crop of material weighing 0.160 g., m.p. 164-5.7°, brought the total yield to 81.8%. The first crop of crystals was recrystallized from hot water, m.p. 169-70°, $[\alpha]_D^{25}$ -65° (c 1.50, 95% ethanol); lit. (89), m.p. 167-8°, $[\alpha]_D^{25}$ -63.0° (c 1.0, 95% ethanol).

The phenyl 2-O-methyl-β-D-glucopyranoside (0.146 g.) was dissolved in 1M aqueous sulfuric acid, and the solution was heated on a steam bath for 2 hr. The reaction mixture was cooled to room temperature, deionized by passage through Amberlite MB-3 (H^+, OH^-) resin, and concentrated to give a colorless sirup (0.083 g.) which crystallized from a mixture of absolute ethanol to give 0.060 g. (57.2%) of material, m.p. 140-55°. Recrystallization from absolute ethanol gave a material whose NMR spectrum, melting and mixed-melting points were identical with those of 2-O-methyl-β-D-glucopyranose (IIc) [see acid-hydrolysis of 1,6-anhydro-2-O-methyl-β-D-glucopyranose (II), (p. 63)].

1,6-ANHYDRO-3-O-ACETYL-β-D-GLUCOPYRANOSE (VIa)

The procedure of Cerny, Gut, and Pacak (33) was used to prepare VIa, m.p. 110-11°; lit. (33), m.p. 111-12.5°.

1,6-ANHYDRO-3-O-ACETYL-2,4-DI-O-METHYL-β-D-GLUCOPYRANOSE (VIb)

1,6-Anhydro-3-O-acetyl-β-D-glucopyranose (VIa) (1.52 g.), was dissolved in warm dichloromethane (40 ml.), the solution cooled to 0°, and boron trifluoride etherate (0.08 ml.) added. To this mixture was added a solution at 0° of diazomethane in dichloroethane (88) until TLC (developer ethyl acetate) showed the

starting material (R_f = 0.45) was completely converted to a new material with a R_f = 0.58. The reaction mixture was filtered to remove polymethylene and the filtrate washed successively with aqueous sodium hydrogen carbonate and water. After drying the solution over sodium sulfate, evaporation of dichloroethane gave a sirup (2.90 g.) which was purified by column chromatography on 80 g. of silica gel with 5:1 ethyl acetate-petroleum ether (b.p. 60-110°) as eluant. The first 300 ml. of eluant was discarded, while the next 700 ml. of eluant was concentrated to give a sirup (1.67 g.). The sirup was dissolved in a mixture of ethyl ether and hexane and the solution cooled to -76° where crystallization occurred to give 1.34 g. of product, m.p. 89-91°. Concentration of the mother liquor gave a second crop of material 0.04 g., m.p. 85-88°. The total yield of 1,6-anhydro-3-O-acetyl-2,4-di-O-methyl-β-D-glucopyranose (VIb) was 80%. Two recrystallizations of the first crop, from isopropyl ether and then from a mixture of acetone, ethyl ether, and hexane, gave the pure product, m.p. 89.5-90.5°, $[\alpha]_D^{31}$ -65.5° (c 1.54, acetone).

Anal. Calc. for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94. Found: C, 52.00; H, 6.75.

1,6-ANHYDRO-2,4-DI-O-METHYL-β-D-GLUCOPYRANOSE (VI)

To a solution of 1,6-anhydro-3-O-acetyl-2,4-di-O-methyl-β-D-glucopyranose (VIb) (1.08 g.) in anhydrous methanol (10 ml.) was added 3 ml. of solution prepared by reacting 0.1 g. of sodium in 10 ml. of anhydrous methanol. The reaction mixture was permitted to remain at room temperature for 40 min., after which water (50 ml.) was added to the mixture. The resulting solution was deionized by passage through Amberlite MB-3 (H^+, OH^-) resin. Evaporation of the effluent gave a light, amber-colored sirup (0.85 g., 96%) which was dissolved in absolute ethanol and decolorized with activated charcoal. The charcoal was removed by filtration, and the filtrate was concentrated to give a colorless sirup which failed to crystallize. The product distilled at 65-74°/0.2-0.3 mm. Hg and had $[\alpha]_D^{26}$ -63.7° (c 3.30 acetone).

Anal. Calc. for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.40; H, 7.24.

1,6-ANHYDRO-2-O-p-TOLUENESULFONYL-β-D-GLUCOPYRANOSE (VIIa)

The method of Cerny, Pacak, and Stanek (34) was employed to prepare VIIa, m.p. 113.5-16.5°; lit. (34), m.p. 117-19°.

1,6-ANHYDRO-3,4-DI-O-METHYL-2-O-p-TOLUENESULFONYL-β-D-GLUCOPYRANOSE

1,6-Anhydro-2-O-p-toluenesulfonyl-β-D-glucopyranose (VIIa), (2.19 g.), freshly prepared silver oxide (6.0 g.), and methyl iodide (30 ml.) were refluxed for 24 hr. after which the silver salts were removed by filtration and washed with a small portion of acetone. The filtrate and acetone washings were combined and concentrated to a sirup. The methylation was then repeated using the described conditions. Crystallization of the amber-colored sirup from a mixture of acetone, isopropyl ether, and hexane at room temperature gave 1.12 g., m.p. 102-4°, of material. Upon concentration of the mother liquor, a second crop of crystals was obtained, 0.31 g., m.p. 95-105°. Total yield of 1,6-anhydro-3,4-di-O-methyl-2-O-p-toluenesulfonyl-β-D-glucopyranose was 1.53 g. (60.0%). Recrystallization of the first crop from the mixed solvent yielded the pure product, m.p. 104-5.5°, $[\alpha]_D^{26}$ -41.9° (c 3.34, methanol); lit. (19), m.p. 105-7°, $[\alpha]_D^{25}$ -34.3° (c 1.2, methanol); lit. (29), m.p. 105-7°, $[\alpha]_D^{22}$ -38 ± 10° (c 0.92, methanol).

1,6-ANHYDRO-3,4-DI-O-METHYL-β-D-GLUCOPYRANOSE (VII)

To a solution of 1,6-anhydro-3,4-di-O-methyl-2-O-p-toluenesulfonyl-β-D-glucopyranose (3.01 g.) in 80% aqueous methanol was added with stirring 33 g. of 5% sodium amalgam. After stirring the reaction mixture for 12 hr., the mercury was removed by filtration and washed three times with water (50 ml.). The aqueous phases were combined, and water was added to bring the total volume to 400 ml. The

resulting solution was deionized by passage through Amberlite MB-3 (H^+, OH^-) resin, and the effluent was concentrated to an amber-colored sirup. Water remaining in the sirup was removed by three successive azeotropic distillations with absolute ethanol. After cooling for several hours at -10°, the anhydrous sirup crystallized to give 1.19 g. (71.6%) of material. Two recrystallizations from a mixture of ethyl ether and hexane yielded pure VII, m.p. 41-3°, $[\alpha]_D^{28}$ -49.7° (c -2.11, acetone); lit. (29), $[\alpha]_D^{24}$ -44 ± 2° (c 1.36, methanol).

Anal. Calc. for $C_8H_{14}O_5$: C, 50.57; H, 7.42. Found: C, 50.63; H, 7.38.

1,6-ANHYDRO-2,3-ISOPROPYLIDENE-β-D-MANNOPYRANOSE (IXb)

Using the procedure of Knauf, et al. (35), five 100-g. charges of ivory nut meal were pyrolyzed to give 50.5 g. (10.1%) of distillate. Using the method of Gasman (36), the distillate was dissolved in anhydrous acetone to which anhydrous copper sulfate (40 g.) was added with stirring followed by concentrated sulfuric acid (3 ml.). After 3 hr. of stirring at room temperature, the copper salts were removed by filtration, and the filtrate was neutralized with an excess of calcium hydroxide (10 g.). Filtration of the calcium salts and concentration of the filtrate yielded 40.5 g. (64.3%) of partially crystalline product. Recrystallization from absolute ethanol gave pure IXb, m.p. 161-2°; lit. (35), m.p. 162°.

1,6-ANHYDRO-β-D-MANNOPYRANOSE (IX)

Removal of the isopropylidene group from 1,6-anhydro-2,3-isopropylidene-β-D-mannopyranose (IXb) was accomplished by the modified procedure of Christensen and Goodman (37). 1,6-Anhydro-2,3-isopropylidene-β-D-mannopyranose (IXb), (6.19 g.), was dissolved in 90% aqueous trifluoroacetic acid (60 ml.), left at room temperature for 10 min., and then concentrated to a sirup. The sirup was dissolved in water (30 ml.), and the resulting solution was deionized by passage through Amberlite

MB-3 (H^+, OH^-) resin. Evaporation of the effluent gave a clear sirup which crystallized with difficulty from hot ethyl acetate to give 4.41 g. (89.0%) of material. Two recrystallizations from a mixture of absolute ethanol and ethyl acetate (3:1) yielded pure IX, m.p. 210.5-11.5°, $[\alpha]_D^{26}$ -129° (c 1.70, H_2O; lit. (35), m.p. 210-11°, $[\alpha]_D$ -127.6° (c 1.50, H_2O).

1,6-ANHYDRO-4-O-(β-D-GLUCOPYRANOSYL)-β-D-GLUCOPYRANOSE (XI)

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-glucopyranose (XIa), (0.962 g.), m.p. 143-4°, $[\alpha]_D^{25}$ -52.8° (c 1.57, chloroform); lit. (90), m.p. 145-6°, $[\alpha]_D^{23}$ -52° (c 3, chloroform), was dissolved in 10 ml. of anhydrous methanol, and to this solution was added 0.03 g. of sodium in 3 ml. of anhydrous methanol. After 40 min. at room temperature, the reaction mixture was diluted with water (50 ml.) and deionized by passage through Amberlite MB-3 (H^+, OH^-) resin. Evaporation of the effluent gave a clear sirup which was dissolved in anhydrous methanol (20 ml.) and freshly distilled n-butanol. Concentration of the solution gave a white hygroscopic material from which the remaining n-butanol was removed, first by passage of dry nitrogen over the surface of the product for 48 hr., and second by drying to constant weight in an Abderhalden drying apparatus for 48 hr. at 62°/0.2 mm. Hg. The yield of XI was 0.302 g. (57.8%), m.p. 98-102°, $[\alpha]_D^{25}$ -74° (c 2.08, water); lit. (42), m.p. 122° (semicrystalline hygroscopic material), $[\alpha]_D^{25}$ -75.0° (c 2, water).

Anal. Calc. for $C_{12}H_{20}O_{10}$: C, 44.45; H, 6.22. Found: C, 44.67; H, 6.31.

The following compounds were supplied through the courtesy of Dr. Paul A. Seib.

1,6-ANHYDRO-2,3-DI-O-METHYL-β-D-GLUCOPYRANOSE (V)

M.p. 43-5°; lit. (38), m.p. 43-5°.

1,6-ANHYDRO-2,3,4-TRI-O-METHYL-β-D-GLUCOPYRANOSE (VIII)

M.p. 62-4°; lit. (39), m.p. 62°.

1,6-ANHYDRO-2-DEOXY-β-D-ARABINO-HEXOPYRANOSE (X)

M.p. 159-60°; lit. (40), m.p. 159-60°.

1,6-ANHYDRO-β-D-GALACTOPYRANOSE (XII)

M.p. 220-3°; lit. (9), m.p. 223-4°.

1,6-ANHYDRO-2-O-METHYL-β-D-GALACTOPYRANOSE (XIII)

M.p. 114-16°; lit. (9, 41), m.p. 115-16°.

1,6-ANHYDRO-4-O-METHYL-β-D-MANNOPYRANOSE (XIV)

$[\alpha]_D^{26}$ -124° (c 0.7, water); lit. (30), $[\alpha]_D^{30}$ -147 (c 0.8, water).

POLYMERIZATION OF 1,6-ANHYDRIDES

Prior to polymerization, the monomers were finely powdered and dried to constant weight in an Abderhalden apparatus over phosphorous pentoxide at room temperature and 0.2 mm. Hg. Polymerizations were performed in Pyrex tubes, O.D. 8 mm. having a length of approximately 15 cm. and sealed at one end. Monomer, 16-30 mg. (40-60 mg. of I), was introduced through a glass funnel which extended to the bottom of the tube.

The catalyst, monochloroacetic acid (MCA), which was purified by sublimation (m.p. 61-4°)*, was dissolved in anhydrous benzene, and an aliquot of solution was

*Reported melting points for the α, β, γ forms of monochloroacetic acid, 62.8°, 56.3°, and 50.7° (91).

pipetted into the polymerization tube to give a mole ratio of monomer to catalyst of 50 to 1. The procedure for the addition of catalyst first involved injecting the aliquot of catalyst in solution into the end of a 25-cm. piece of Pyrex tubing, O.D. 2 mm., with a Hamilton (1-10 µl.) syringe (No. 701, ± 1% accuracy and precision, Hamilton Company, Whittier, California). Into the other end of the catalyst tube was injected approximately 10 µl. of anhydrous benzene. The polymerization tube was held horizontally and the catalyst tube carefully inserted with the end containing the catalyst going in first. The assemblage of tubes was tipped to about 45°, permitting the solution of catalyst and benzene wash to flow onto the monomer. The operations for the addition of catalyst are illustrated schematically in Fig. 6. The eyedropper cap (Drummon Scientific Company, Broomoll, Pennsylvania) shown in Fig. 6 aided initially in getting the liquids to flow.

To remove the benzene, the polymerization tube was placed in a desiccator for 1 hr. at room temperature under reduced pressure ($\approx$ 93 mm. Hg). The desiccator contained beakers of phosphorous pentoxide and MCA to keep the moisture content low and to minimize the loss of catalyst from the polymerization tube by sublimation. Titration of the tube contents after benzene removal showed that 95-7% of the catalyst remained. The titration techniques employed will shortly be discussed (p. 82). The mole ratio of monomer to MCA after this loss of catalyst ranged from 54:1 to 51:1.

After evaporation of benzene, the polymerization tube was sealed over a flame 1-2 cm. from the open end. The tube was immersed in an oil bath with the end of the tube containing monomer and catalyst approximately 12 cm. below the surface of the oil. The oil bath was maintained at 115 ± 1° by a Fenwall thermostat.

The tube, after a specified polymerization time, was removed from the oil bath and permitted to cool to room temperature. The reaction mixture was dissolved in

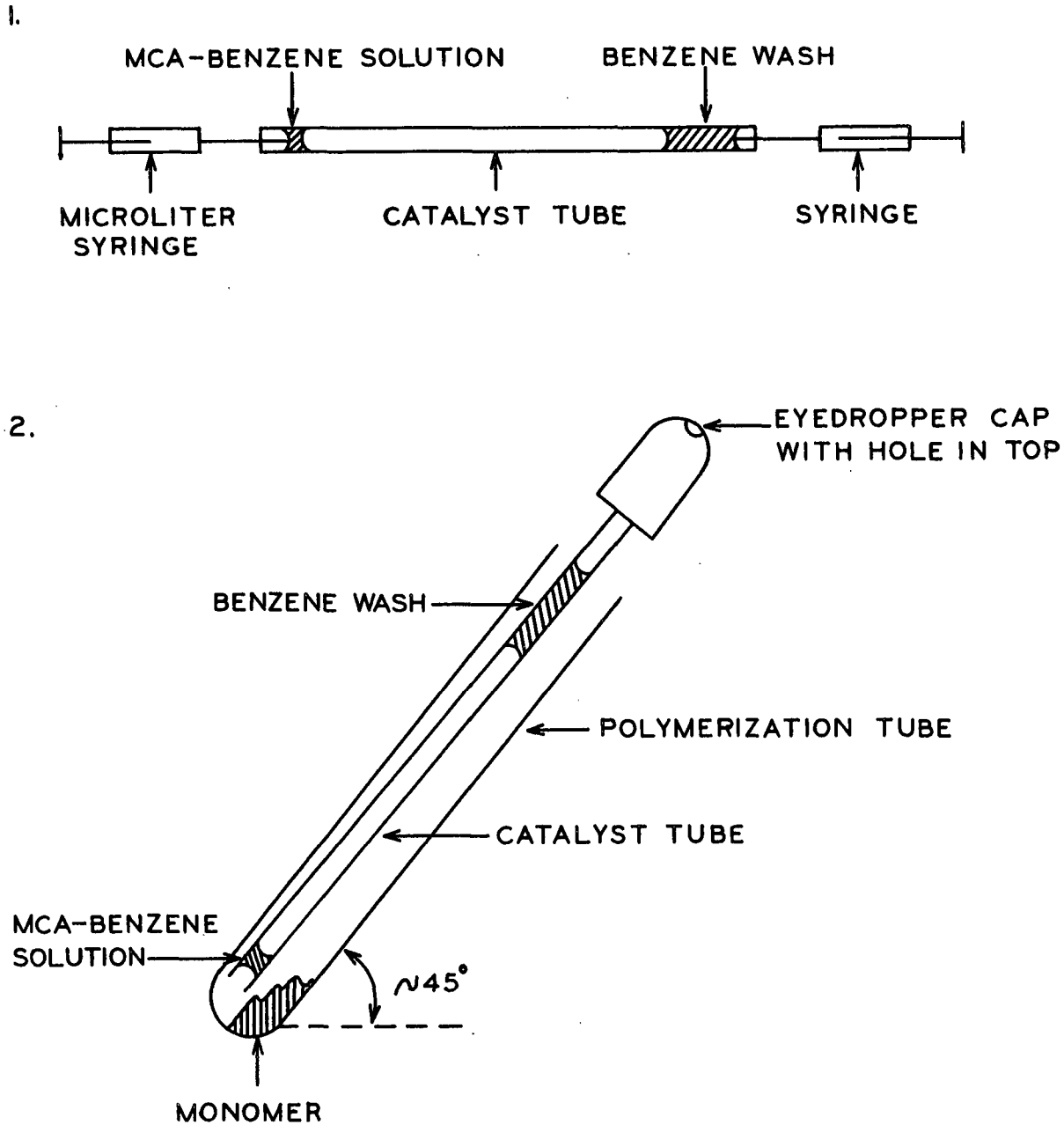


Figure 6. Method of Addition of Monochloroacetic Acid Catalyst to Monomer

water containing methyl α-D-mannopyranoside, which was used as an internal standard for the GLC determination of monomer. o-Hydroxymethylphenyl-β-D-glucopyranoside (salicin) was used as internal standard for Compound XI. When the volume of internal standard solution to be added was greater than 0.1 ml., a 1.00-ml. pipet (± 0.005 ml., Pyrex, Corning Glass Works) was employed, but for volumes less than 0.1 ml., a 0.05-ml. Hamilton Syringe (No. 705N, ± 1% accuracy and precision) was used. The tube was shaken to dissolve the reaction mixture, and the solution was transferred quantitatively to a 50-ml. round-bottom flask with 30 ml. of absolute ethanol. The solution was then evaporated to dryness. To determine the amount of monomer remaining, a reaction mixture containing internal standard was first trimethylsilylated with the commercial silylating agent, TRI-SIL (Pierce Chemical Company, Rockford, Illinois). The silylated mixture of 1-3 µl. was injected into the gas chromatograph three times to give three chromatograms.

The fraction of monomer remaining in the polymerization reaction was calculated using the equation

$$F_M = f(V_{IS})(C_{IS})(1/W_{M_o})(\langle A_M/A_{IS}\rangle) \qquad (3)$$

where

F_M = the weight fraction of monomer in the reaction mixture

f = response factor for internal standard relative to monomer

V_{IS} = volume of internal standard, ml.

C_{IS} = concentration of internal standard, g./ml.

W_{M_o} = weight of initial monomer, g.

$\langle A_M/A_{IS}\rangle$ = ratio of areas, average gas chromatographic responses, for monomer and internal standard

The value of f is calculated from gas chromatographic responses of monomer and internal standard in mixtures of known composition. Response factors were

determined at three levels of monomer concentration; these were approximately 25, 50, and 75 weight percent. In Table XI, the retention times and the response factors are given for all monomers.

TABLE XI

RETENTION TIMES[a] AND RESPONSE FACTORS FOR TRIMETHYLSILYLATED 1,6-ANHYDRO SUGARS

1,6-Anhydro Sugar	Retention Time, min.	Response Factor[b]
Levoglucosan (I)	5.2	1.04 ± 0.01
Levogalactosan (XII)	4.3	1.05 ± 0.01
Levomannosan (IX)	4.6	1.01 ± 0.02
2-Deoxylevoglucosan[c] (X)	2.8	1.13 ± 0.01
2-O-Methyllevoglucosan (II)	3.5	1.37 ± 0.01
3-O-Methyllevoglucosan (III)	3.2	1.32 ± 0.02
4-O-Methyllevoglucosan (IV)	3.7	1.40 ± 0.01
2-O-Methyllevogalactosan (XIII)	3.2	1.33 ± 0.01
3,4-Di-O-methyllevoglucosan (VII)	2.4	1.45 ± 0.01
Methyl α-D-mannoside	7.6, 12.0[c]	--
Cellobiosan[d] (XI)	6.5	1.23 ± 0.01
Salicin[d]	4.6	--

[a]Column temperature 170-5°; injection port temperature 250°.
[b]Determined at three different weight fractions of monomer, see text.
[c]Column temperature 164-7°; injection port temperature 250°.
[d]Column temperature 260-5°; injection port temperature 325°.

All analyses were performed on an Aerograph Hy-Fi gas chromatograph (Model A-600-B) equipped with a hydrogen flame ionization detector. The column (5') employed was housed in 1/8-inch stainless steel tubing and contained 5% W/W SE-30 on 60/80 mesh

Chromosorb W. Dry nitrogen was used as the carrier gas at a pressure of 12 lb.; the hydrogen flow rate to the detector was approximately 30 ml./min.

The area under the monomer and the internal standard curves were integrated manually with a Technicon integrator/calculator (Model AAG, Technicon Chromatography Corp., Ardsley, New York). The integrator was adjusted (Internal Standard setting 5.00) to give the maximum number of counts per square centimeter of curve integrated. This number of counts per square centimeter (18.0 counts/cm.^{2}) remained constant during integration of the curves.

For each injection into the gas chromatograph, the monomer and internal standard curves were integrated four times to give the average number of counts per curve. The procedure was repeated for the other two injections, and the three area ratios averaged to obtain an average gas chromatographic response, $\left\langle \underline{A}_{\underline{M}}/\underline{A}_{\underline{IS}} \right\rangle$. The relative precision of $\left\langle \underline{A}_{\underline{M}}/\underline{A}_{\underline{IS}} \right\rangle$ was found to vary between 1 and 3%.

In Appendix V, the polymerization data for the 1,6-anhydrides and D-glucopyranose are presented. Those mixtures of monomer and catalyst which were not heated to 115° were used as controls to check the reliability of the GLC determinations in each polymerization run. The reproducibility in two separate polymerization runs on I was found to be ± 3% up to 6 hr. reaction time ($\underline{F}_{\underline{M}} = 0.45$). (Table XVII, Appendix V).

DETERMINATION OF CATALYST LOSS

A small loss of MCA occurred (3 to 5%) on evaporation of the benzene prior to polymerization, while after prolonged polymerization time, a major loss was observed. To determine how much catalyst was lost at these times, reaction mixtures were dissolved in approximately 10 ml. of distilled water, and the solutions were titrated with standard sodium hydroxide solution.

A Beckman glass electrode pH meter (Model H-2, Beckman Instruments, South Pasadena, California) was employed to obtain a titration curve. The procedure for finding the end point (92) involved plotting the pH of the solution as a function of the volume of standard base solution added. Next, a smooth curve was drawn through the points and the steepest tangent drawn on the curve. This tangent coincided with the curve over a finite distance, and the end point was chosen as the volume at the midpoint of the region of contact. Titrations were performed with a Kimax automatic buret (No. 17132F, $\pm$ 0.01 ml., Owens-Illinois). In Fig. 7 is presented a typical titration curve as an example for determination of the end point. Table XII shows the data for the loss of MCA upon evaporation of benzene prior to polymerization and, also, as a function of polymerization time. All data were obtained on I with the exception of the last determination, Experiment No. 10, which was done using Compound (IX).

Small amounts of benzene present in the mixture do not affect the polymerization reaction as is shown in the polymerization of I (Table XVII, Footnote b, Appendix V).

DETECTION OF POLYMER

The polymerizates of all monomers having a F_M of 0.5 were qualitatively examined by paper, thin-layer, and gas-liquid chromatography. All polymerizates gave spots at the origin and spots for oligomers. Because similar results were obtained for all the polymerizates, only the data for the polymerizate of I will be given in detail.

The polymerizate of I after being dissolved in a small amount of water was spotted on a paper chromatogram (Whatman No. 1 paper, 57-cm. length). The chromatogram was developed for 8 days in a mixture of butyl acetate, pyridine, ethanol, and water (8:2:2:1) by the descending method. Detection of the compounds on the chromatogram was accomplished with silver nitrate using the dip procedure (93). At the end of 8 days of development monomer (I) was eluted from the end of the chromatogram.

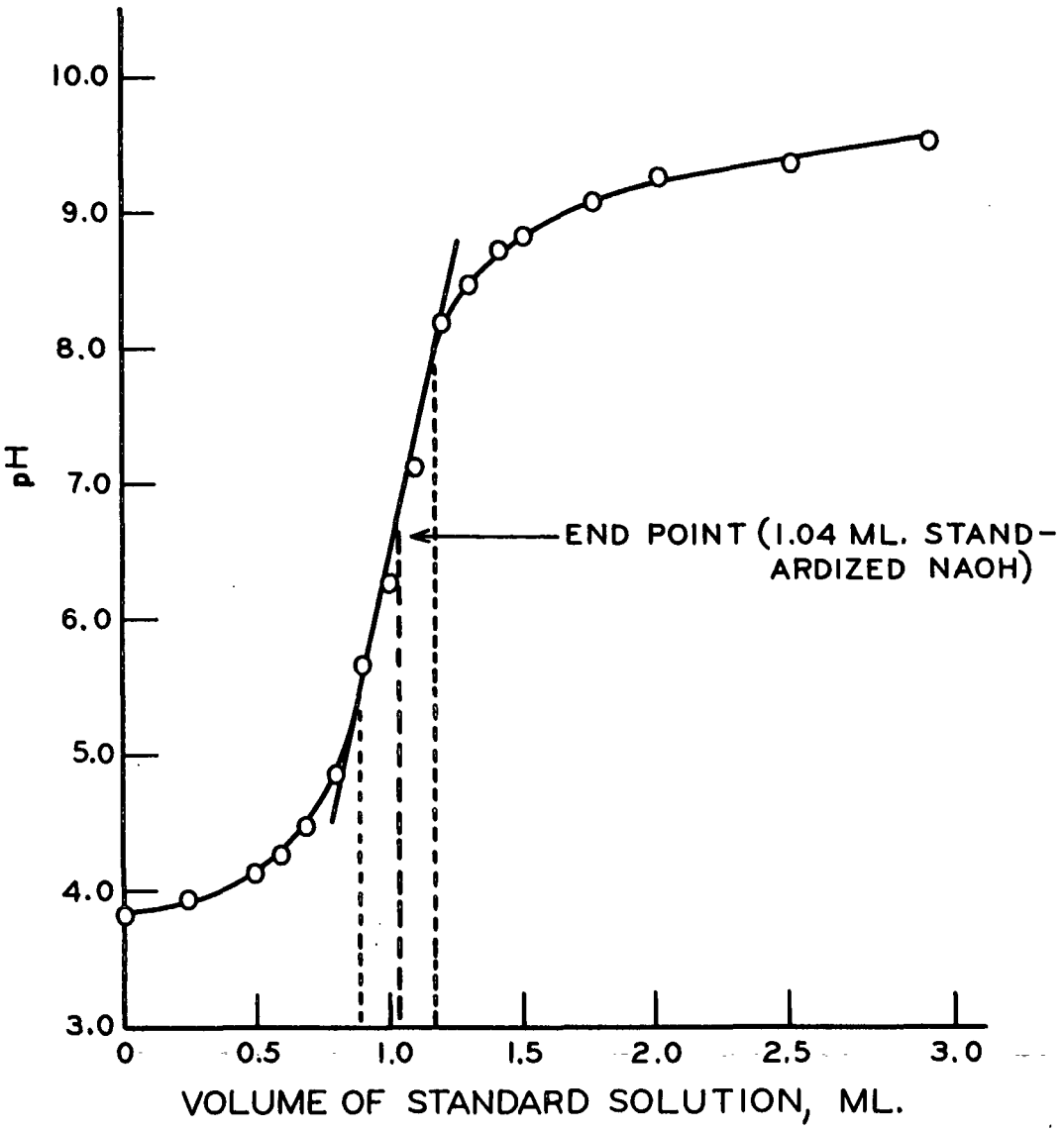


Figure 7. Titration Curve for MCA Lost During Evaporation of Benzene; See Experiment 1, Table XII

TABLE XII

DATA FOR LOSS OF MCA CATALYST DURING EVAPORATION OF BENZENE AND DURING POLYMERIZATION

Experiment No.	Polymerization Time, hr.	Added W_{MCA}, x 10^{-4} g.	V_{NaOH}, ml.[d]	Titrated W_{MCA}, x 10^{-4} g.	Titrated W_{MCA} / Added W_{MCA}
1[a]	--	4.31	1.04	4.07	0.95
2[a]	--	2.78	0.68	2.7	0.97
3[b]	3.0	3.06	0.73	2.9	0.95
4[b]	4.0	4.17	1.02	3.99	0.96
5[b]	4.7	4.17	1.00	3.91	0.94
6[b]	6.1	4.31	1.00	3.91	0.91
7[b]	16.0	4.03	0.60	2.4	0.60
8[b]	16.0	3.89	0.55	2.2	0.57
9[b]	16.0	4.17	0.59	2.3	0.55
10[c]	16.0	2.64	0.46	1.8	0.68

[a] Data for weight MCA loss during benzene removal from levoglucosan.

[b] Data for weight MCA loss during polymerization of levoglucosan at 115°.

[c] Data for weight MCA loss during polymerization of levomannosan.

[d] 0.00414M NaOH.

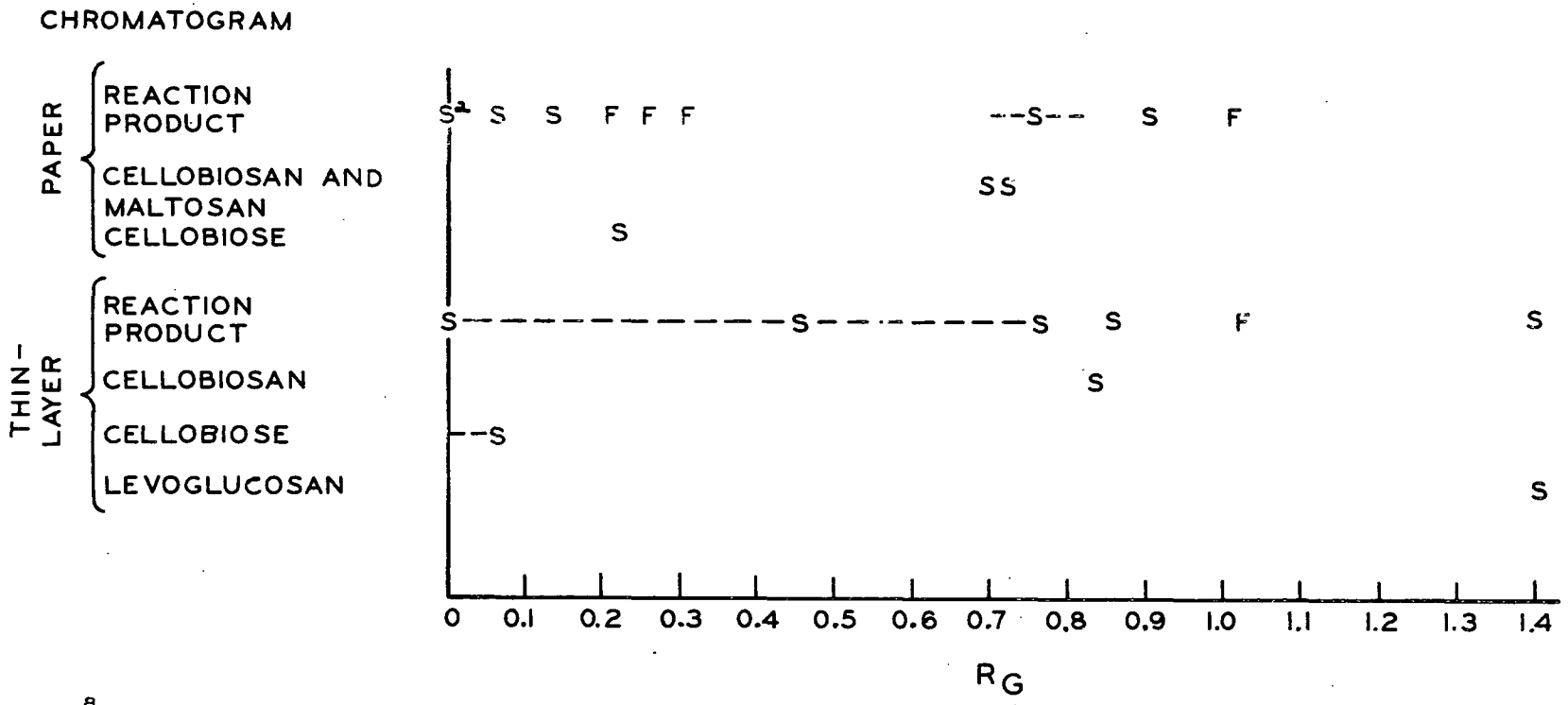
The polymerizate solution was also spotted on a thin-layer plate (200 x 100 mm.) coated to a thickness of 1 mm. with silica gel G (Brinkmann Instruments). The plates were developed twice with a mixture of ethyl acetate and methanol (2:1). The components of the polymerizate were visualized by spraying the plate with a 10% solution of sulfuric acid in methanol followed by charring on a hot plate.

The results from the paper and thin-layer chromatograms are illustrated in Fig. 8.

A small portion of the polymerizate was trimethylsilylated with TRI-SIL and the mixture analyzed by GLC for oligomers. The gas chromatograph was operated with a column temperature of 260-5° and an injection port temperature of 325°. A broad peak with its center having a retention time of 6.3 min. was observed for the polymerizate of I. Cellobiosan and maltosan gave sharp peaks with retention times of 6.5 and 5.7 min., respectively. It was concluded on the basis of chromatographic evidence that oligomer and higher molecular weight materials were present in the polymerizates of I.

LARGE-SCALE POLYMERIZATION OF 1,6-ANHYDRO-2-O-METHYL-β-D-GLUCOPYRANOSE (II) FOR $\bar{M}n$ and $[\alpha]_D$ DETERMINATION

1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II) (0.320 g.) was heated for 16 days at 115° with a mole ratio of monomer to MCA of 52 to 1, and the dark amber-colored product was dissolved in approximately 10 ml. of water. When acetone (50 ml.) was added to the aqueous solution, an amber-colored substance precipitated. After centrifugation, the precipitate was washed with acetone (50 ml.) on the centrifuge. Thin-layer chromatography (developer ethyl acetate-methanol 2:1) showed that only polymeric material was present (all material remained at the starting line). The precipitated polymer was dissolved in several milliliters of water and the solution lyophilized. The yield of 2-methyl-D-glucan was 0.116 g. (36%), $[\alpha]_D^{25}$ +79.2° (c 1.91, water), $\bar{M}n$ 1030 (by vapor pressure osmometry, ArRo Laboratories, Inc., Joliet, Illinois).



[a]S = spot, F = faint spot, -- = streaking.

Figure 8. R_G Values for 1,6-Anhydro-β-D-glucopyranose (I) Polymerizate as Determined by Paper and Thin-Layer Chromatography

ACID-HYDROLYSIS OF 2-O-METHYL-D-GLUCAN AND 2-DEOXY-D-GLUCAN

2-O-Methyl-D-glucan

1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II) (0.0456 g.) was heated for 12 days at 115° with MCA as catalyst at a mole ratio of monomer to catalyst of 51 to 1. The polymerizate was dissolved in distilled water (15 ml.) and the solution dialyzed in 3 liters of distilled water for 2 hr. The dialyzate was evaporated to dryness to give a material weighing 0.028 g. Thin-layer chromatography of this material (developer, ethyl acetate — methanol 2:1) showed dialysis was incomplete in removing all the monomer from the polymerizate. The material was further fractionated by dissolving it in methanol (1 ml.) and adding acetone (20 ml.) to precipitate a light amber-colored substance which was removed by centrifugation. The precipitate was washed with acetone (20 ml.) on the centrifuge and was dried; yield 0.006 g. (13%). Thin-layer chromatography showed only high molecular weight material which remained on the starting line.

The precipitated polymer was hydrolyzed by refluxing in 0.2M sulfuric acid (20 ml.) for 72 hr. The hydrolyzate was cooled to room temperature, deionized by passage through Amberlite MB-3 (H^+, OH^-) resin, and the effluent concentrated to sirup. The major component indicated by paper chromatography was 2-O-methyl-D-glucopyranose (R_G 1.8) along with four minor components. Chromatograms were developed in a mixture of ethyl acetate, pyridine, and water (8:2:1) and compounds detected by silver nitrate-sodium-hydroxide-sodium thiosulfate (93) and p-anisidine hydrochloride reagents (94), respectively.

2-Deoxy-D-glucan

1,6-Anhydro-2-deoxy-β-D-arabino-hexopyranose (X), (0.0228 g.), was heated for 4 hr. at 115° with MCA present in the mole ratio of monomer to catalyst, 52:1. The product was dissolved in 3 ml. of hot (80°) water, and the polymer was precipitated

by the addition of acetone (10 ml.). The precipitated substance was separated by centrifugation, twice washed with acetone (20 ml.) on the centrifuge, and dried; yield 0.013 g. (58%). Thin-layer chromatography of this substance (developer, ethyl acetate — methanol 2:1) showed only polymeric material which remained on the starting line.

The polymer was hydrolyzed in 0.5M sulfuric acid (10 ml.) at room temperature for 2 hr. followed by 1/2 hr. at 50°. The hydrolyzate was diluted with water (10 ml.), neutralized by passage through Amberlite MB-3 (H^+, OH^-) resin, and the effluent evaporated to a sirup. The major component identified by TLC (developer, ethyl acetate — methanol 2:1) was 2-deoxy-D-arabino-hexose (R_G 2.0).

The polymer hydrolyzate was acetylated in the usual manner using pyridine (0.2 ml.) and acetic anhydride (0.16 ml.). The sirupy acetylated product (13 mg.) was anomerized with acid to give principally the α-pyranose form using the procedure outlined by Bonner (95). To the sirup dissolved in 0.1 ml. of a mixture of acetic acid and acetic anhydride (1:1) was added 5 ml. of 0.5M sulfuric acid solution. The reaction mixture was allowed to stand at room temperature and was neutralized with an aqueous sodium hydrogen carbonate at 4°. This mixture was stirred for 30 min. and was extracted three times with chloroform (30 ml.). The chloroform phase after successive washings with an aqueous sodium hydrogen carbonate and water, and drying over sodium sulfate was evaporated to give a sirup (10 mg.). Crystallization occurred from a mixture of isopropyl alcohol and petroleum ether (b.p. 30-60°) to give 5 mg. of product, m.p. 107-9°. A mixed-melting point with authentic material (m.p. 108-9°) obtained by the procedure of Bonner was undepressed.

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APPENDIX I

THE MECHANISM OF THE PYROLYTIC DEGRADATION OF 2-O-METHYLCELLULOSE (IIa)

The thermal degradation of 2-O-methylcellulose to 1,6-anhydro-2-O-methyl-β-D-glucopyranose indicates that a 1,2-anhydro-4-O-substituted-α-D-glucopyranose is probably not an intermediate in the pyrolysis of cellulose, although several investigators have suggested this (96). In the absence of solvent molecules, pyrolysis is assumed to proceed by an ionic mechanism, wherein a concerted process appears favorable, since charge dispersal in the transition state cannot be stabilized by the solvent molecules. Anchimeric assistance by the oxygen on the C-2 atom, however, does not seem likely, since three-membered, oxonium ion rings rarely occur (97). Winstein, et al. (98) have found that methoxyl groups do not anchimerically assist a leaving group if the transition state would consist of a three-membered, cyclic methyloxonium ion. Olah and Bollinger (99), in their work on stable carbonium ions, have presented evidence that bridged methyl oxonium ion formation does not occur in the ionization of 2-halo-3-methoxy-2,3-dimethyl butanes. In addition, no evidence of C-2 participation via a bridged, benzyl-oxonium ion was found by Ishikawa and Fletcher (100) in the methanolysis of 2-O-benzyl-3,4,6-tri-O-p-nitrobenzoyl-β-D-glucopyranoxyl bromide. On the other hand, anchimeric assistance by a methoxyl group is favorable when the cyclic intermediate is five-membered (101). Numerous examples of five-membered, oxonium-ion intermediates have been reported (102).

In the pyrolysis of cellulose, Kilzer and Broido (103) postulated the formation of 1,4-anhydro-α-D-glucopyranose, a five-membered cyclic intermediate and its subsequent rearrangement to 1,6-anhydro-β-D-glucopyranose. The thermal degradation (35) of a β-1,4 linked mannan gives 1,6-anhydro-β-D-mannopyranose, again probably through a 1,4-anhydro intermediate, since the reacting groups on carbon atoms C-1 and C-2 cannot assume a trans-diaxial arrangement. Lemieux (104) proposed the same

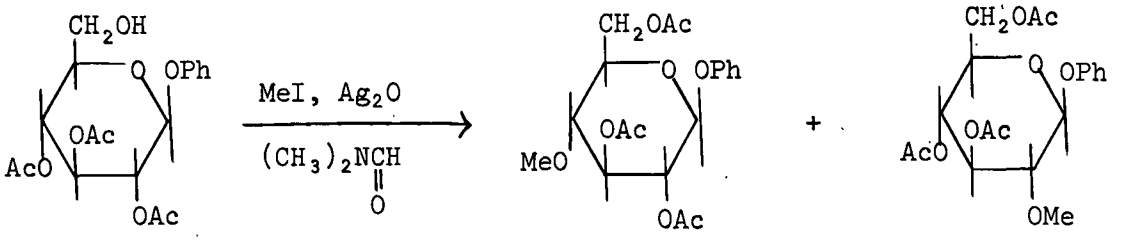
intermediate in the alkaline transformation of phenyl β-D-mannopyranoside to 1,6-anhydro-β-D-mannopyranose. Stable 1,4-anhydro derivatives of hexoses have been isolated (105), including 1,4-anhydro-2,3,6-tri-O-methyl-α-D-glucopyranose (106) prepared by the pyrolysis of 2,3,6-tri-O-methyl cellulose.

Based on considerable evidence favoring five-membered and not three-membered cyclic carbonium ions and on the isolation of 1,6-anhydro-2-O-methyl-β-D-glucopyranose from the pyrolysis of 2-O-methyl-β-D-cellulose, it is more plausible that 2-O-methyl cellulose (IIa) and probably cellulose degrade thermally through 1,4-anhydro-intermediates.

APPENDIX II

PREPARATION OF PHENYL 2,3,6-TRI-O-ACETYL-4-O-METHYL-β-D-GLUCOPYRANOSIDE (IVa)

The preparation of phenyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranose (IVa) was accomplished by three routes. In the first route, Compound (IVa) was prepared in quantity in 56% yield by the reaction of phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranose (IVc) at room temperature with methyl iodide and silver oxide in N,N-dimethylformamide. On concentration of the mother liquor from this reaction mixture, a second crystalline compound, subsequently identified as phenyl 3,4,6-tri-O-acetyl-2-O-methyl-β-D-glucopyranoside (IVd), was obtained in 29% yield. Identification of IVd was accomplished by deacetylation of this compound with sodium methoxide in methanol followed by acid hydrolysis to give 2-O-methyl-β-D-glucopyranose whose spectrum, melting and mixed-melting points were identical to an authentic sample.

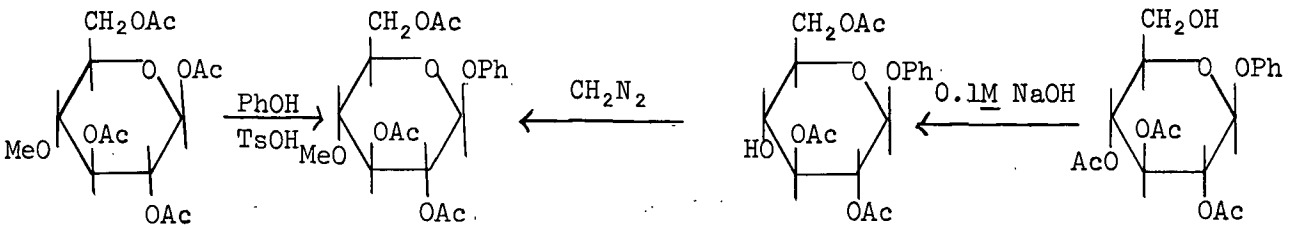


IVc IVa IVd

Acetyl migration around the pyranose ring has been observed in the methylation of methyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (107). Refluxing this derivative in methyl iodide containing silver oxide led to a 30% yield of crystalline methyl 3,4,6-tri-O-acetyl-2-O-methyl-β-D-glucopyranoside. No attempt was made to isolate the 4-methyl ether derivative. Bouveng, et al. (108) showed, however, that methylation with methyl iodide and silver oxide in N,N-dimethylformamide at room temperature

gave methyl 2,3,6-tri-O-acetyl-4-O-methyl-β-D-glucopyranoside in 45% yield. He further showed that the hydrolyzate of the mother liquor contained only a trace of the 2-methyl ether. These results indicate that the addition of N,N-dimethylformamide accelerates the methylation of the 4-hydroxyl more than the migration of an acetyl group to the C-4 position.

In the work reported herein, Compound (IVa) was identified through the remaining two routes. The second route involved condensation of known 1,2,3,6-tetra-O-acetyl-4-O-methyl-β-D-glucopyranose (IVe) (31) with phenol in the presence of p-toluenesulfonic acid monohydrate (TSOH) to give IVa in 51% yield. The third route entailed reaction of phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (IVc) in 0.1M aqueous sodium hydroxide to give phenyl 2,3,6-tri-O-acetyl-β-D-glucopyranoside (IVf) which, on methylation with diazomethane, gave IVa in 42% yield.

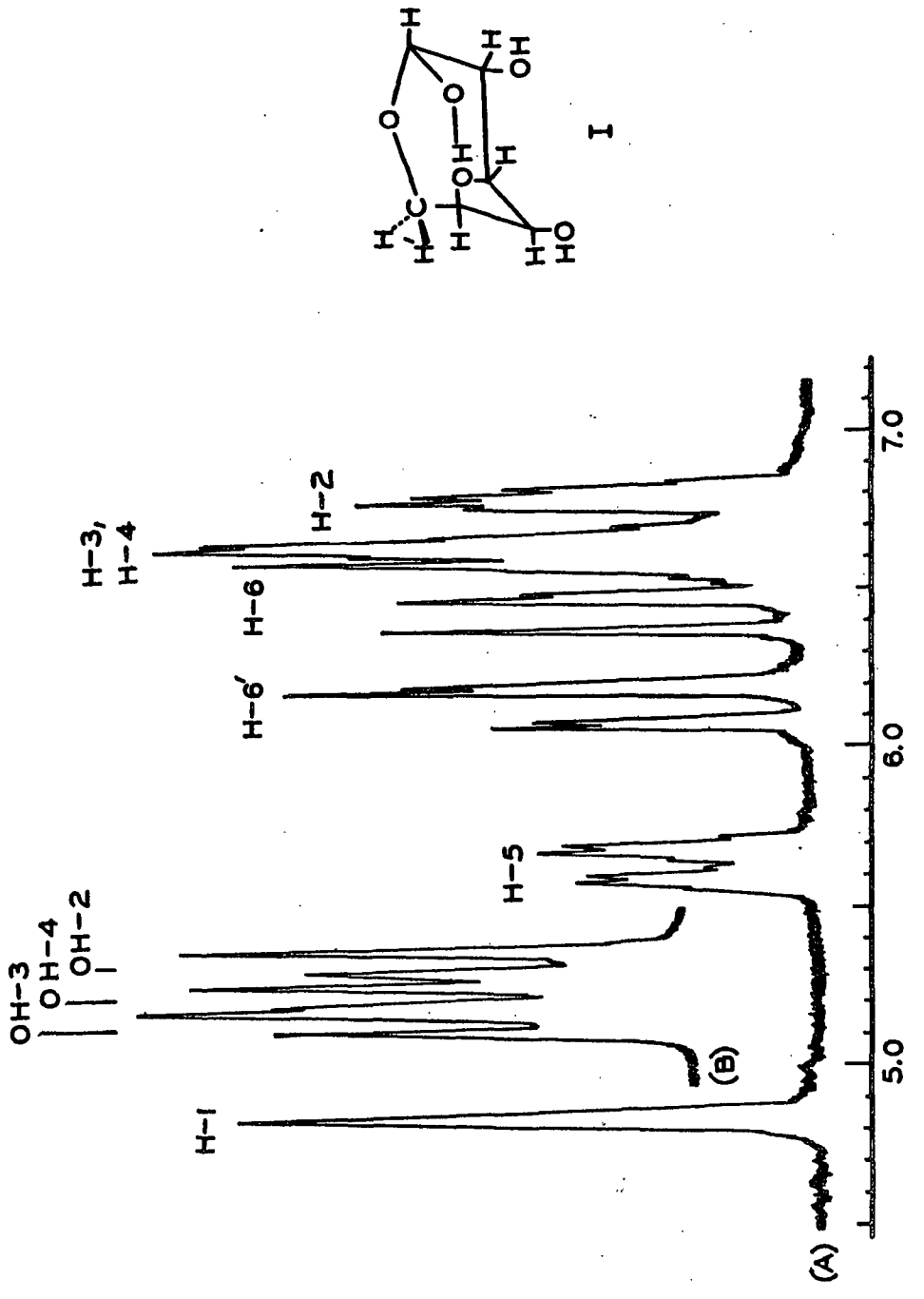


IVe IVa IVf IVc

Rearrangement of IVc in the presence of weak alkali solution was first performed by Helferich and Strauss (32). They were, however, unsure of the rearranged product. In an analogous system, acetyl migration from the C-4 atom to the C-6 atoms occurs when 1,2,3,4-tetra-O-acetyl-β-D-glucopyranose is dissolved in weak, aqueous alkali (109). Since methylation of IVf with diazomethane, is known not to cause acetyl migration (31), the product isolated by Helferich and Strauss was thus identified as phenyl 2,3,6-tri-O-acetyl-β-D-glucopyranoside.

APPENDIX III

NUCLEAR MAGNETIC RESONANCE SPECTRA OF 1,6-ANHYDRIDES



I

Figure 9. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-β-D-glucopyranose (I) in Methyl Sulfoxide-d_6 with Trace of Hydrogen Chloride Present, and (B) Partial Spectrum in Methyl Sulfoxide-d_6

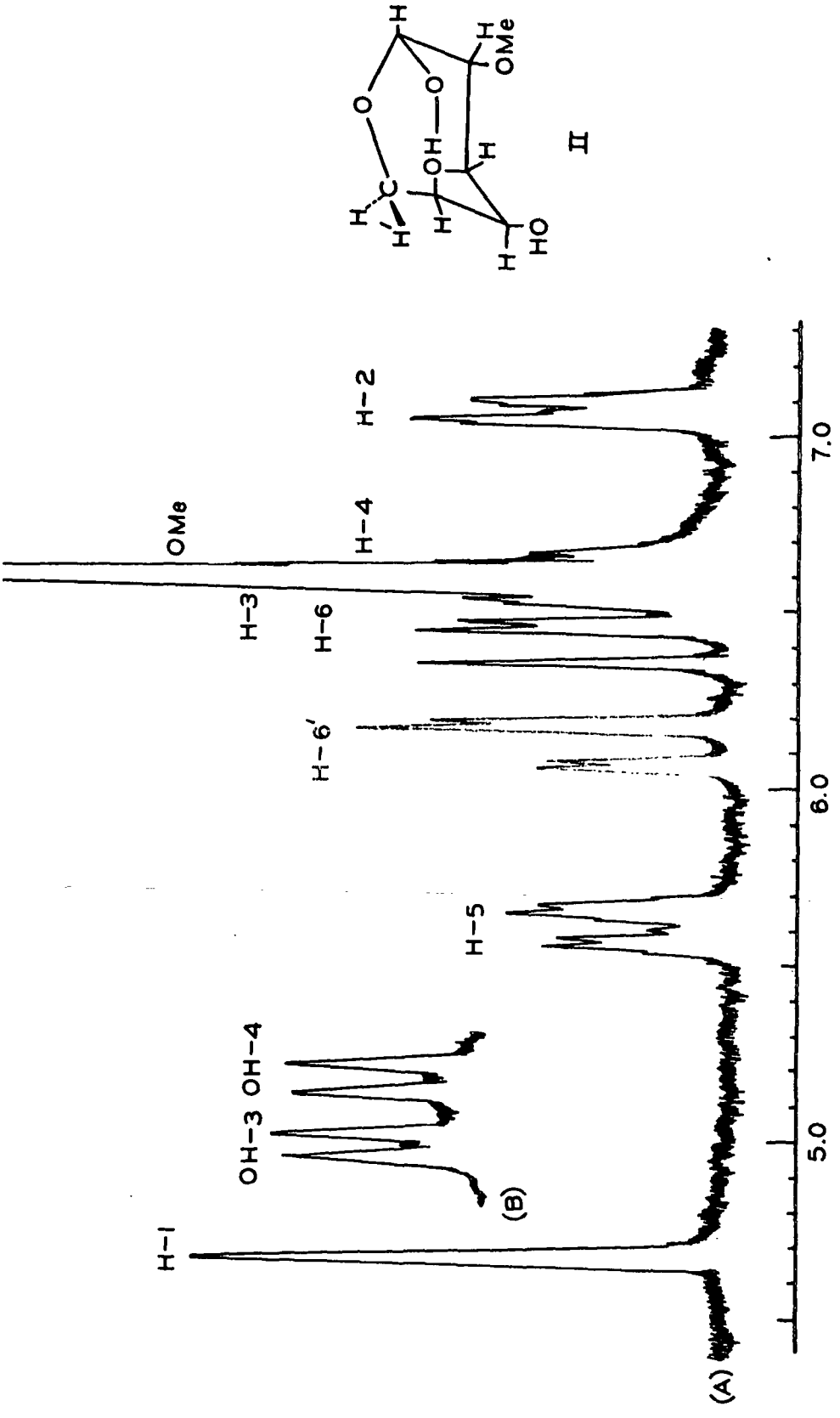


Figure 10. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II) in Methyl Sulfoxide-$\underline{d}_6$ with Trace of Hydrogen Chloride Present, and (B) Partial Spectrum in Methyl Sulfoxide-$\underline{d}_6$

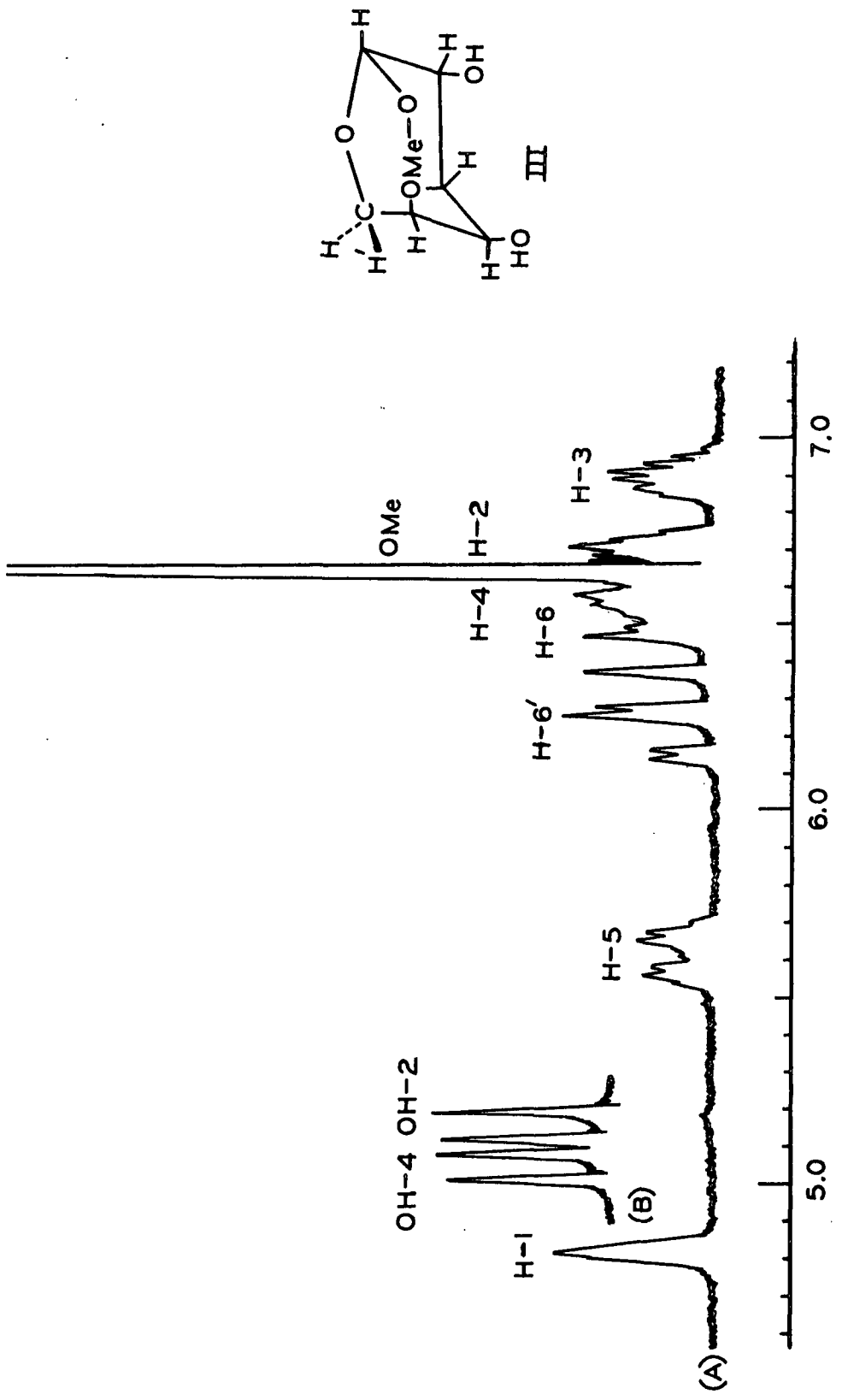


Figure 11. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-3-O-methyl-β-D-glucopyranose (III) in Methyl Sulfoxide-d_6 with Trace of Hydrogen Chloride Present, and (B) Partial Spectrum in Methyl Sulfoxide-d_6

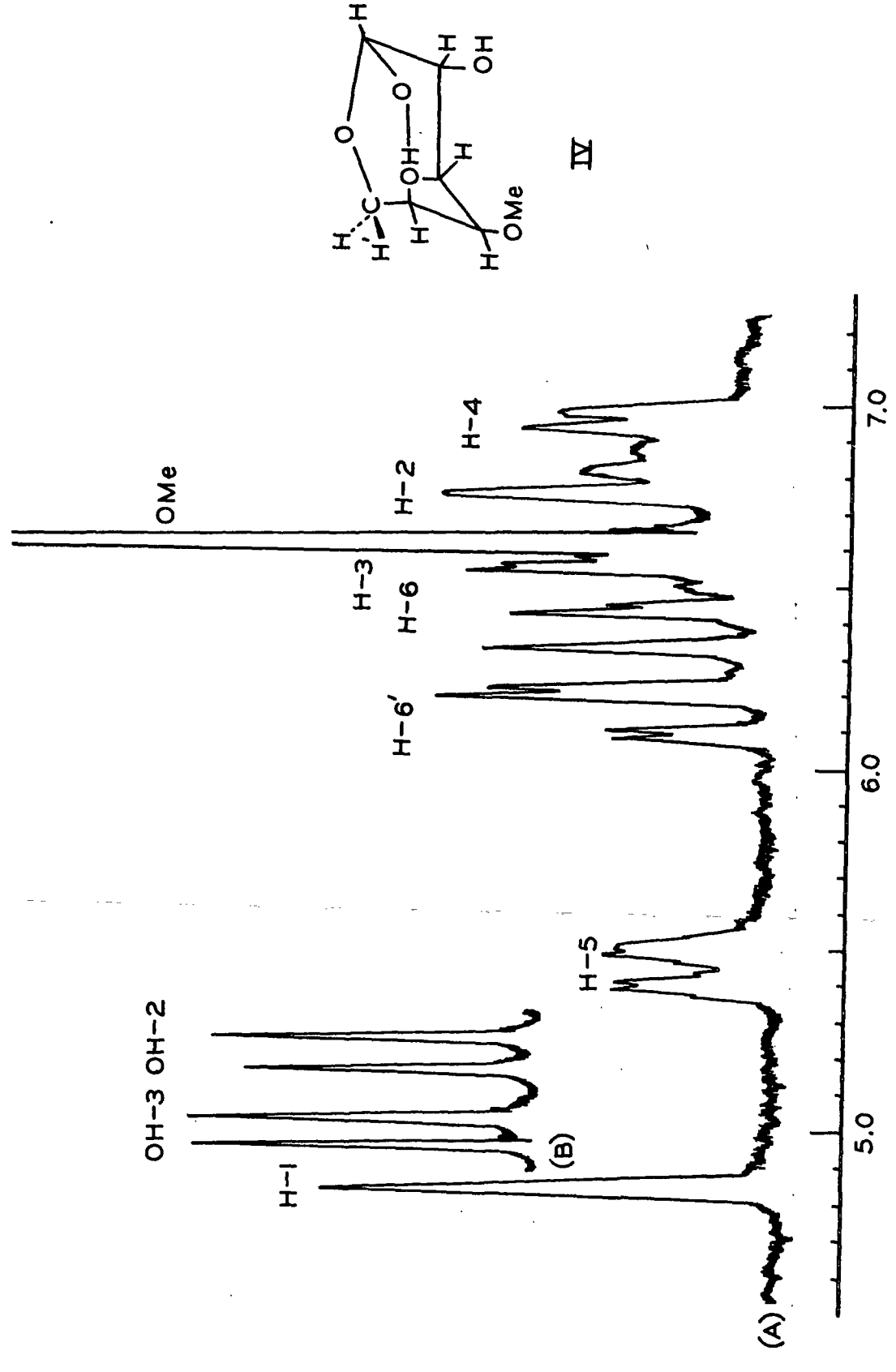


Figure 12. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-4-O-methyl-β-D-glucopyranose (IV) in Methyl Sulfoxide-d_6 with Trace of Hydrogen Chloride Present; and (B) Partial Spectrum in Methyl Sulfoxide-d_6

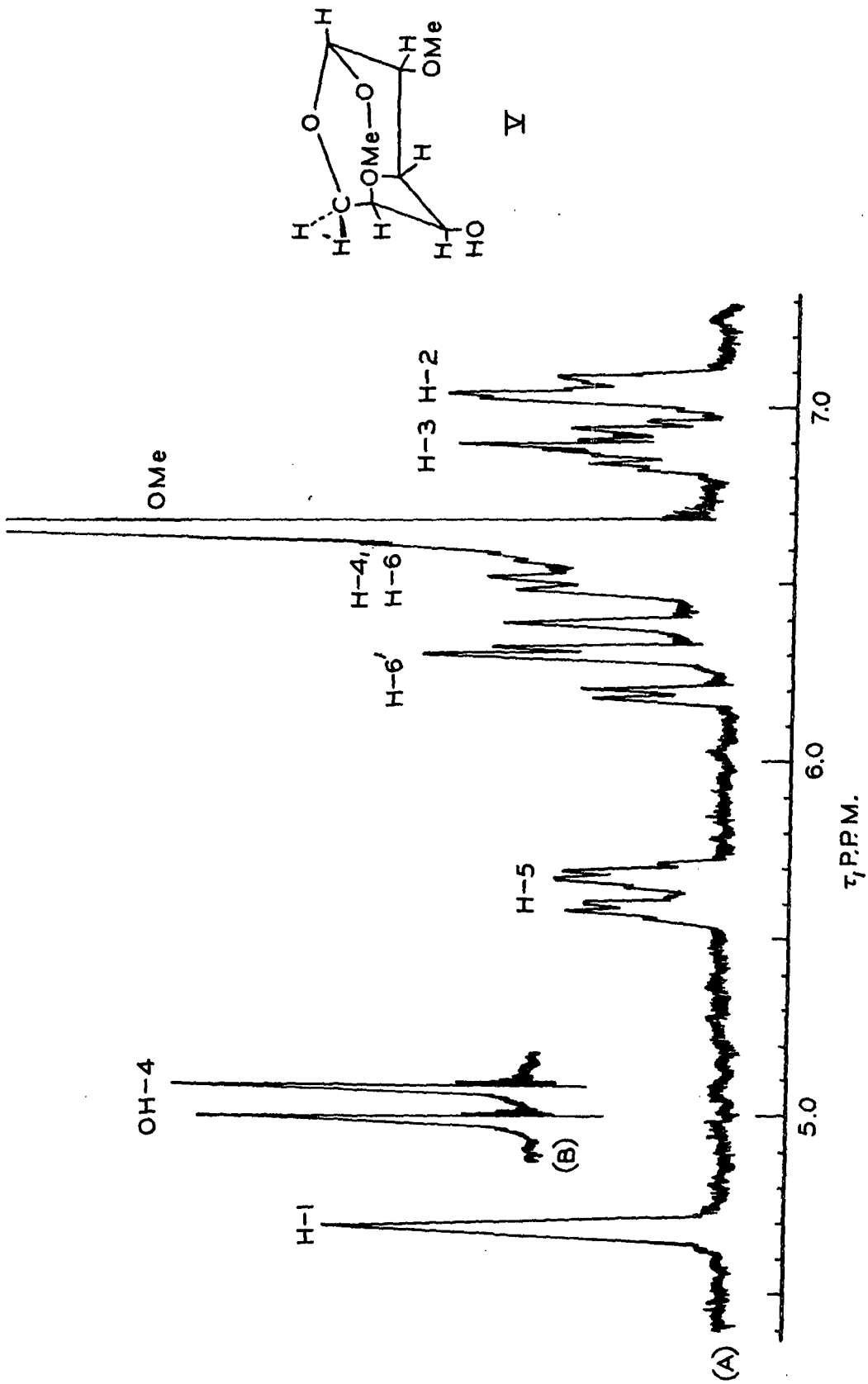


Figure 13. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-2,3-di-O-methyl-β-D-glucopyranose (V) in Methyl Sulfoxide-$\underline{d}_6$ with Trace of Hydrogen Chloride Present, and (B) Partial Spectrum in Methyl Sulfoxide-$\underline{d}_6$

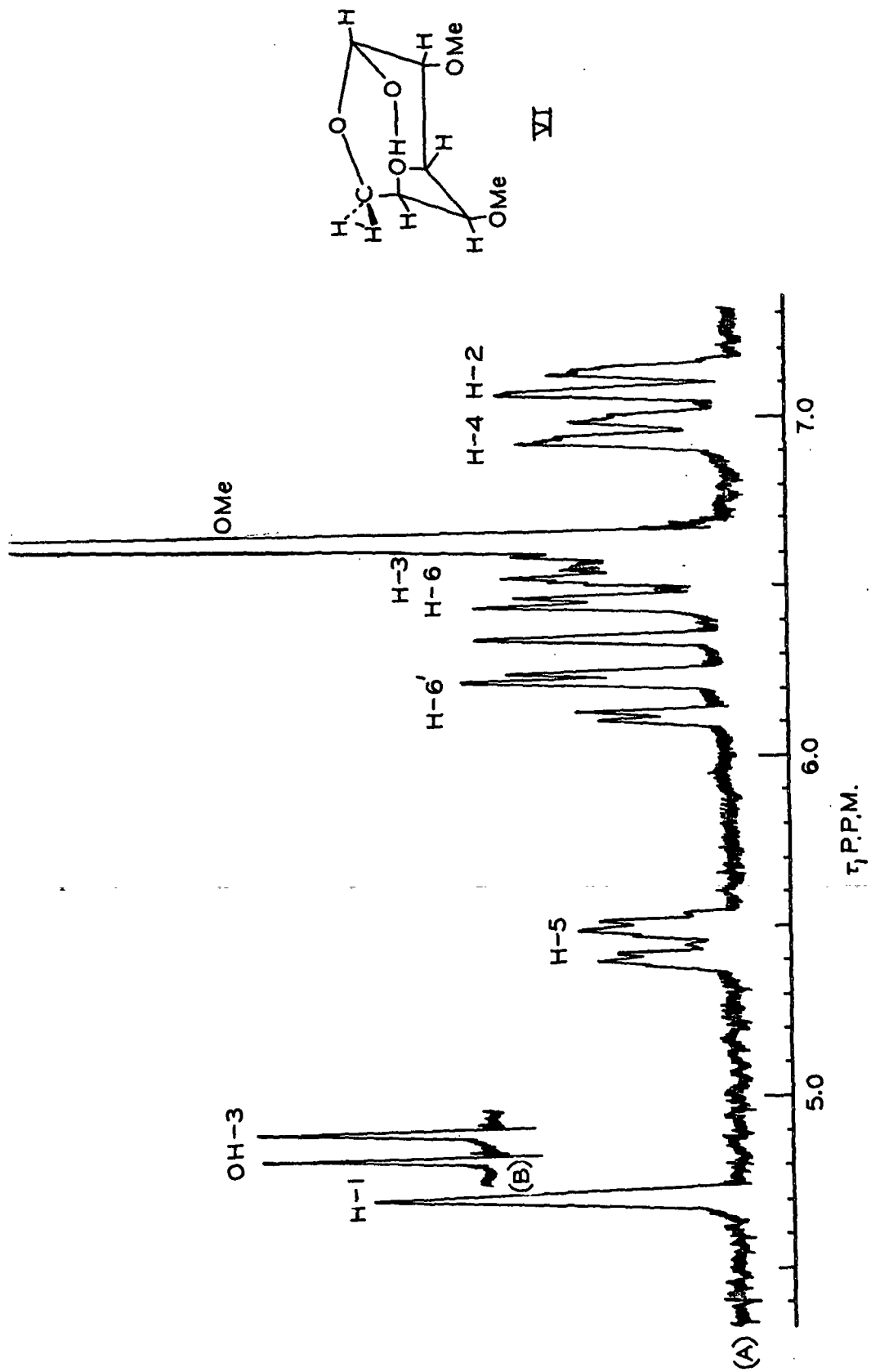


Figure 14. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-2,4-di-O-methyl-β-D-glucopyranose (VI) in Methyl Sulfoxide-$\underline{d}_6$ with Trace of Hydrogen Chloride Present, and (B) Partial Spectrum in Methyl Sulfoxide-$\underline{d}_6$

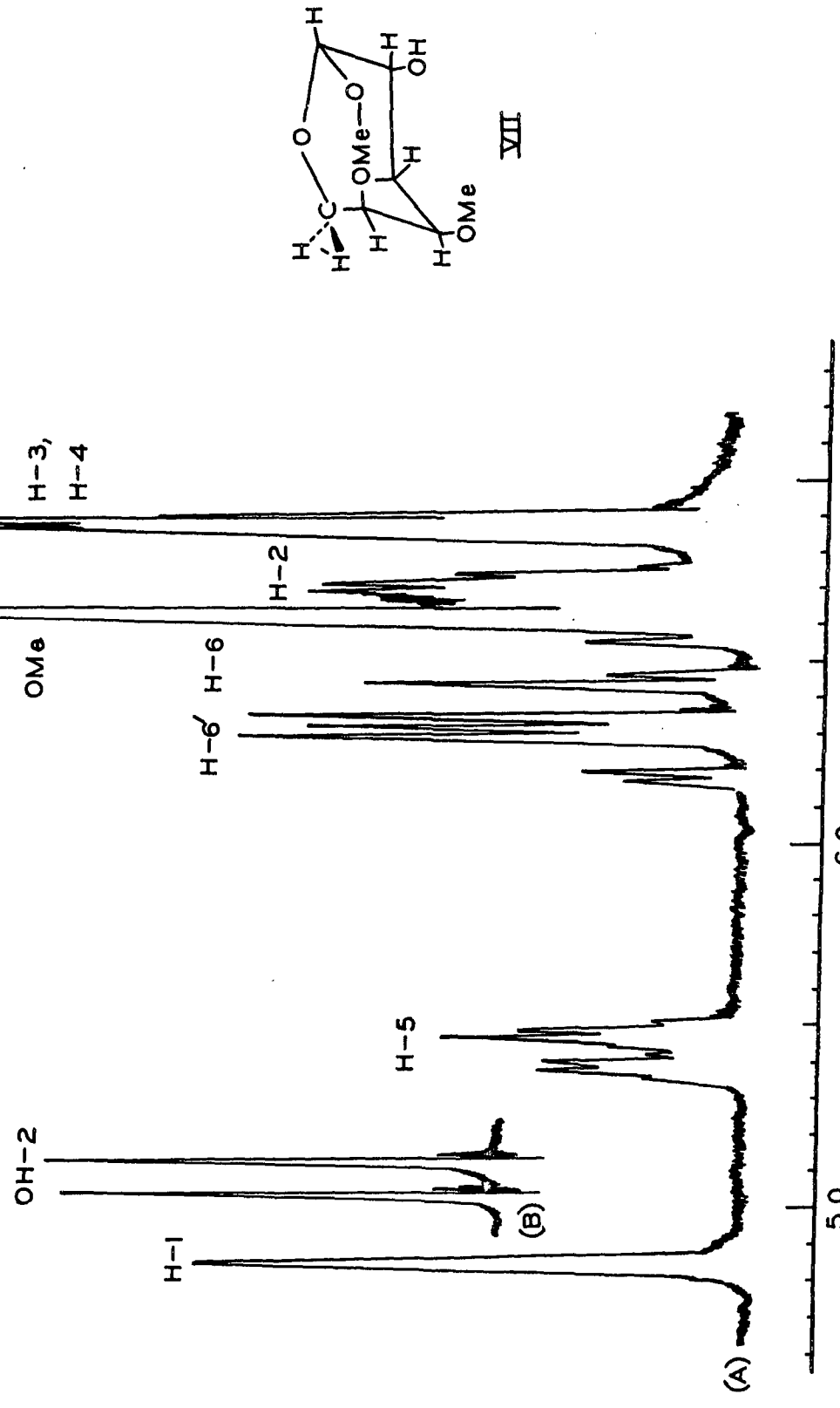


Figure 15. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-3,4-di-O-methyl-β-D-glucopyranose (VII) in Methyl Sulfoxide-$\underline{d}_6$ with Trace of Hydrogen Chloride Present, and (B) Partial Spectrum in Methyl Sulfoxide-$\underline{d}_6$

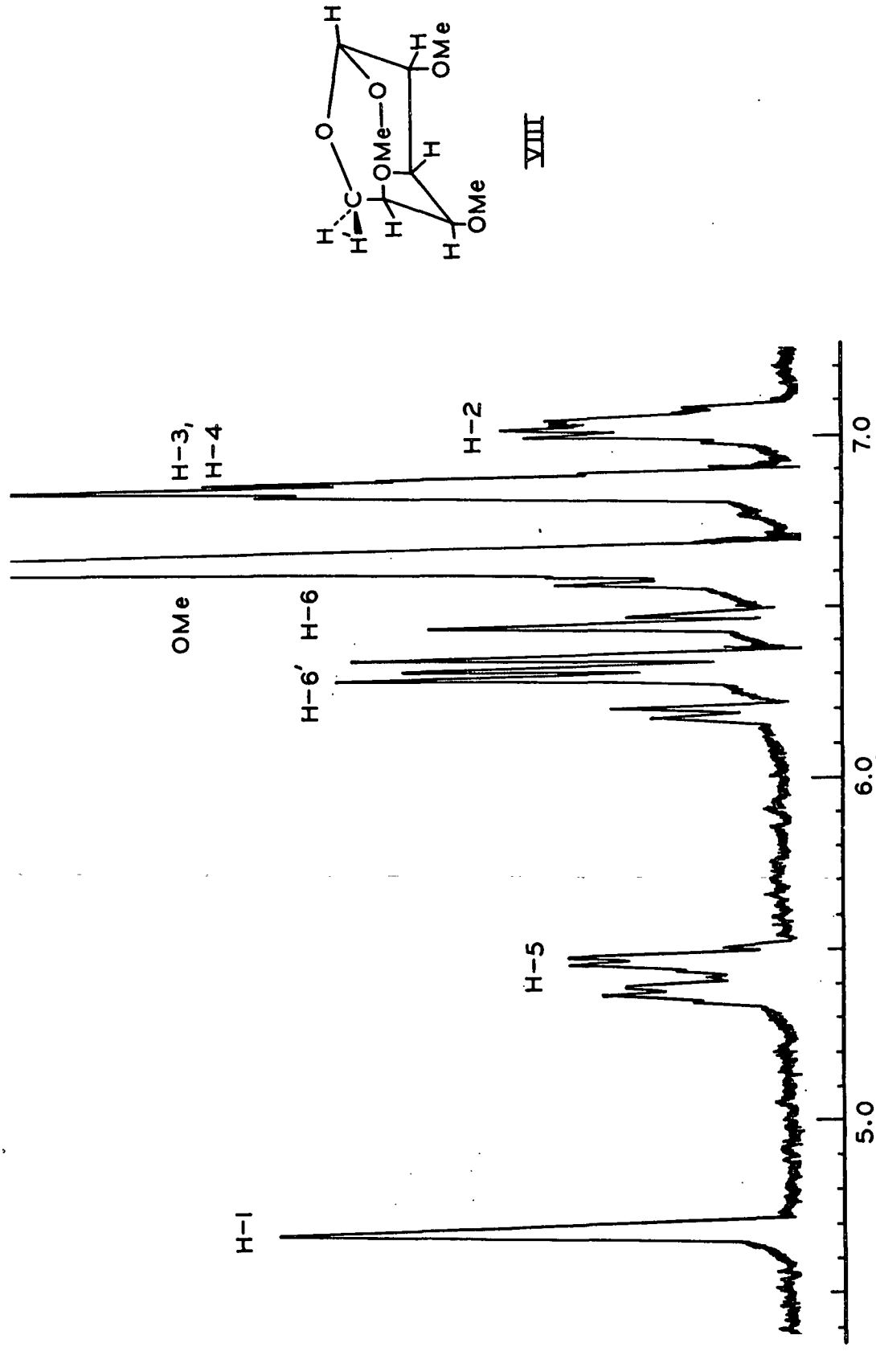
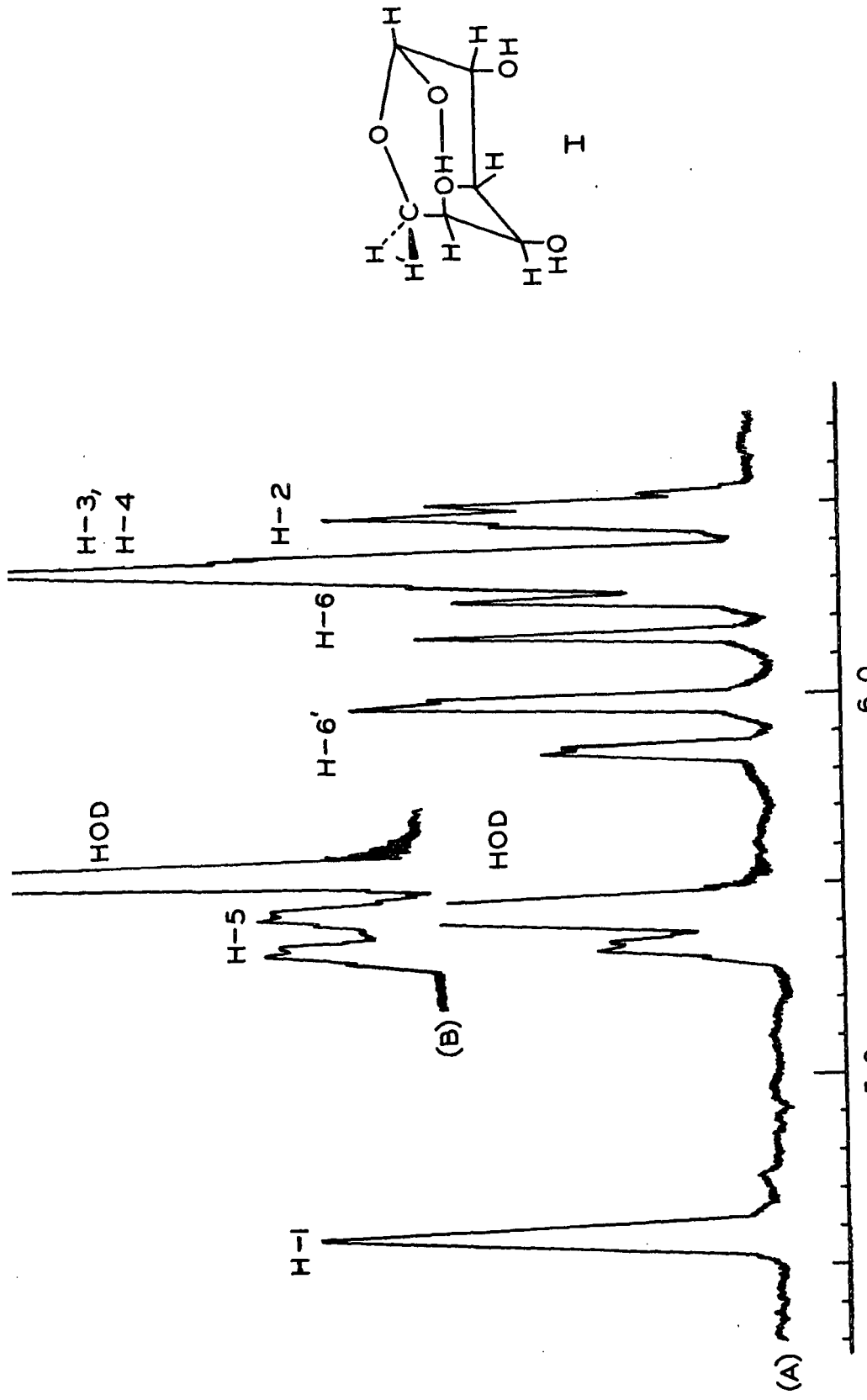


Figure 16. NMR Spectrum (60 MHz) of 1,6-Anhydro-2,3,4-tri-O-methyl-β-D-glucopyranose (VIII) in Methyl Sulfoxide-d_6 with Trace of Hydrogen Chloride Present



I

Figure 17. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-β-D-glucopyranose (I) in Deuterium Oxide, and (B) Partial Spectrum in Hot Deuterium Oxide

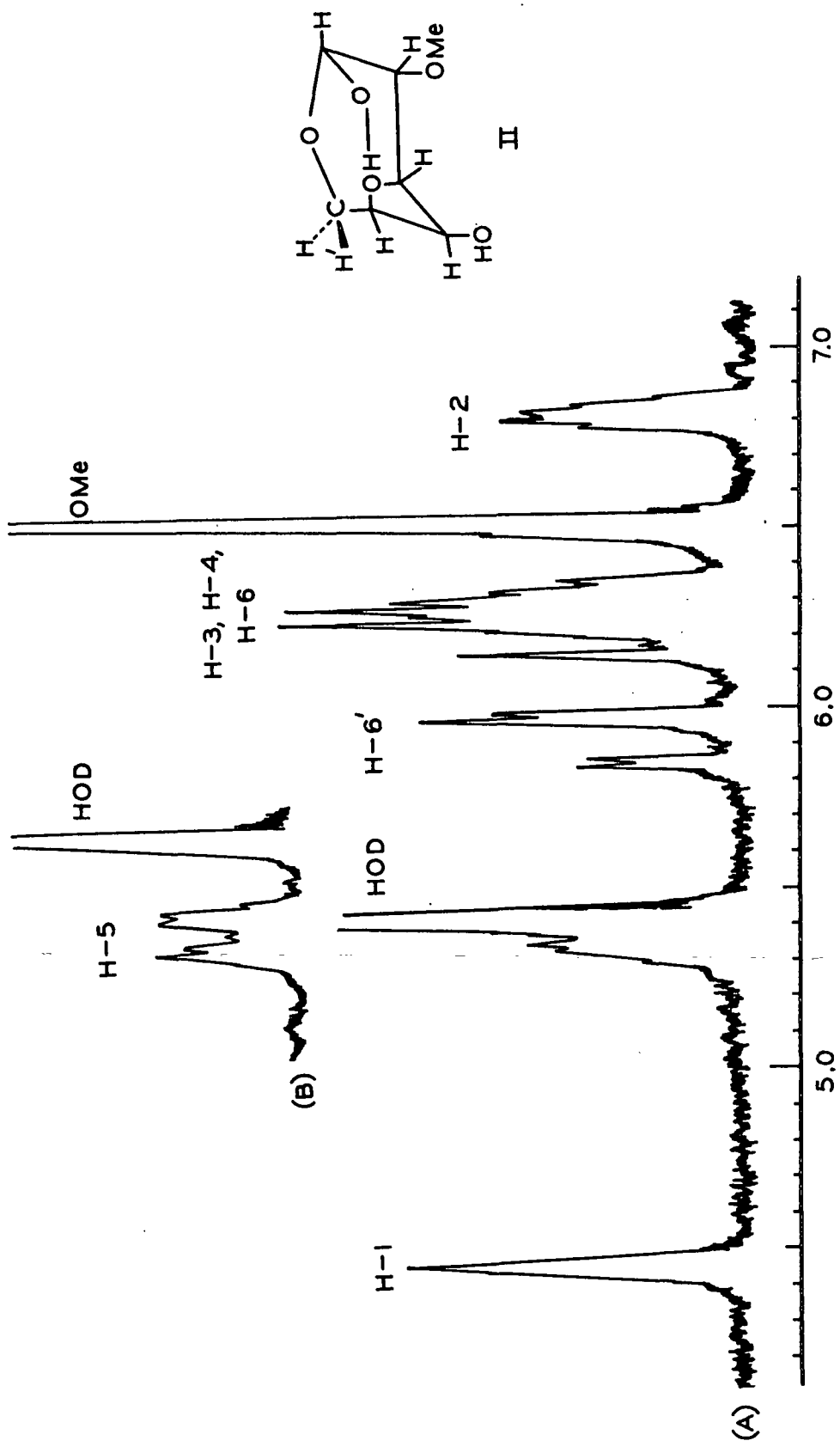


Figure 18. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II) in Deuterium Oxide, and (B) Partial Spectrum in Hot Deuterium Oxide

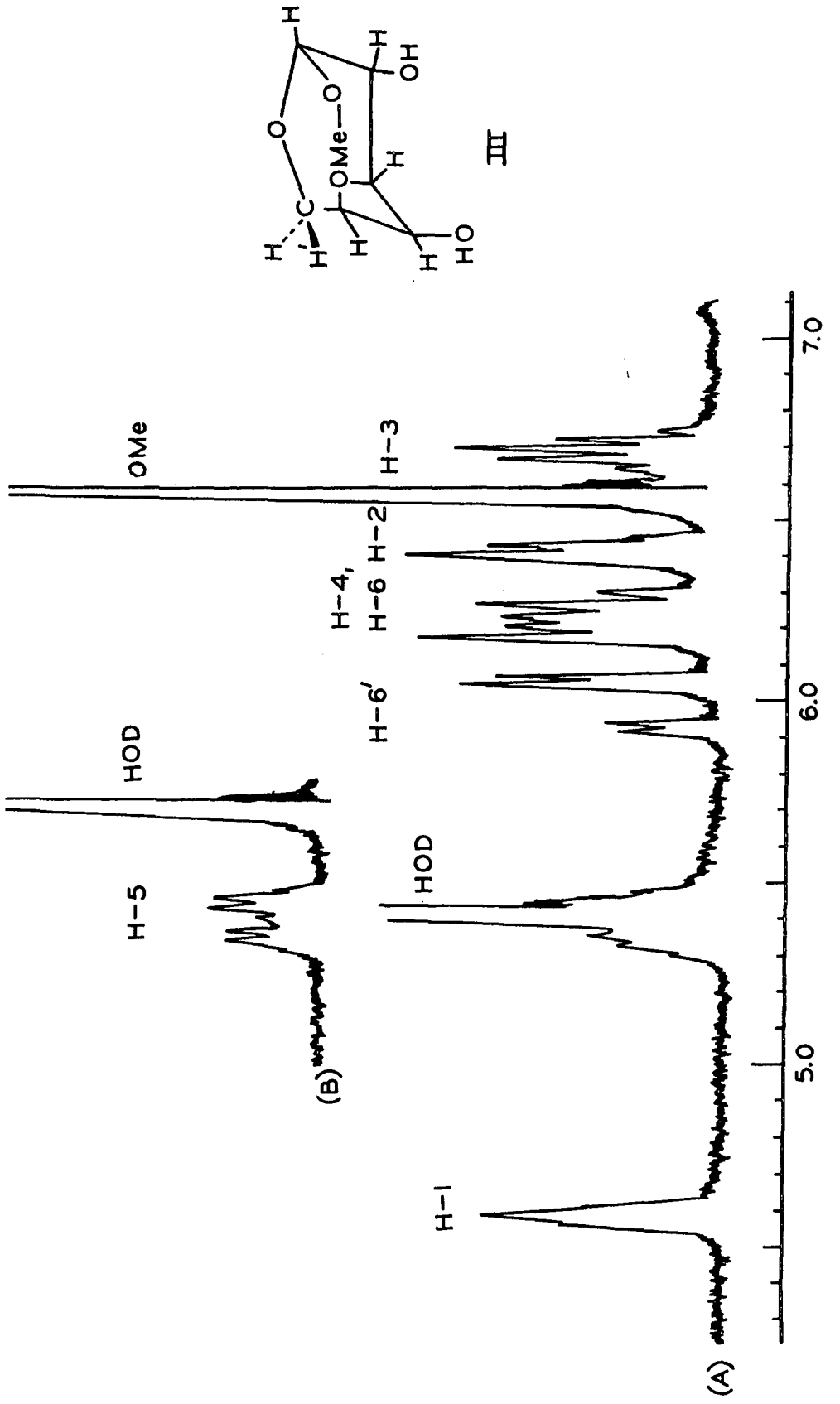


Figure 19. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-3-O-methyl-β-D-glucopyranose (III) in Deuterium Oxide, and (B) Partial Spectrum in Hot Deuterium Oxide

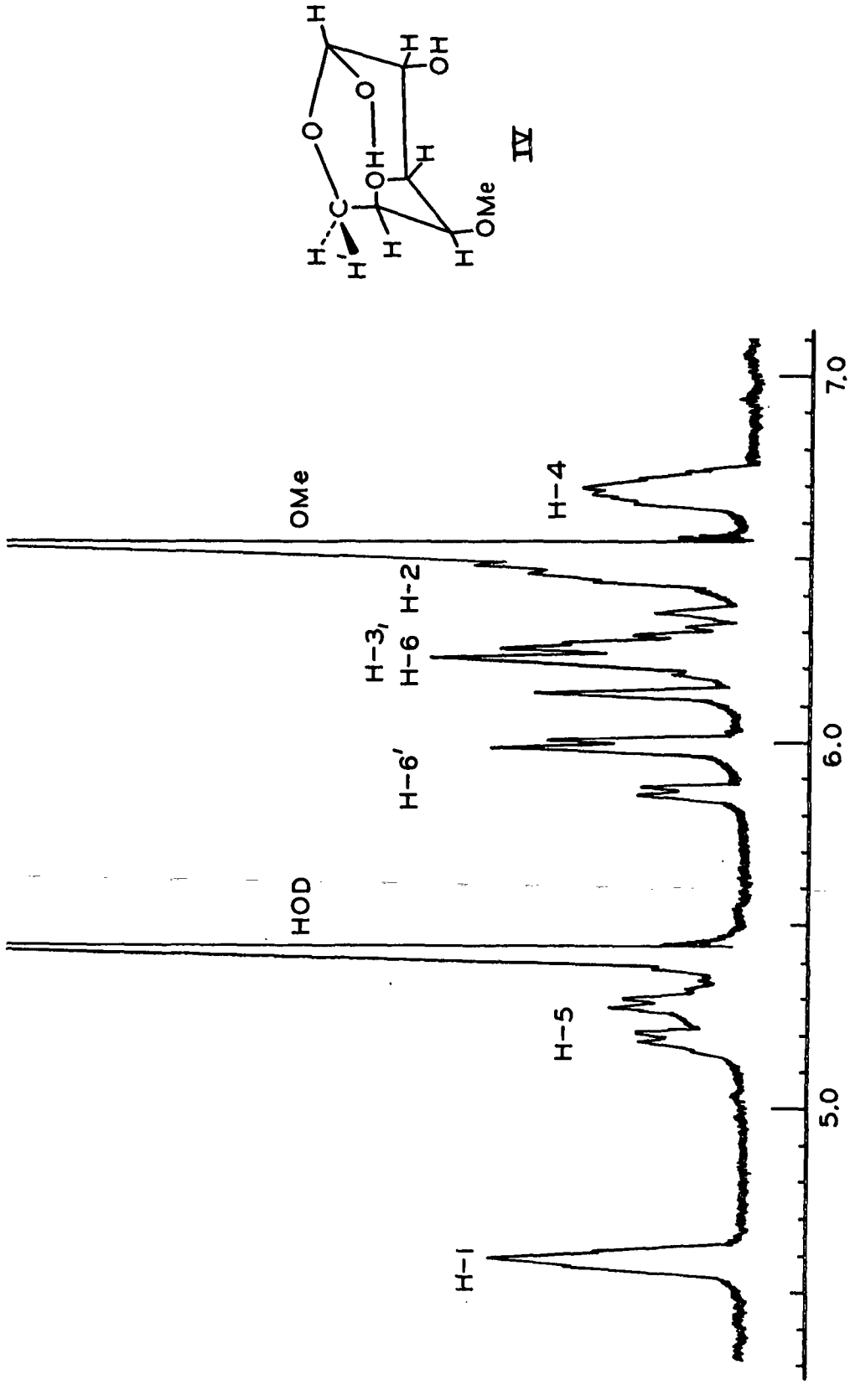


Figure 20. NMR Spectrum (60 MHz) of 1,6-Anhydro-4-O-methyl-β-D-glucopyranose (IV) in Deuterium Oxide

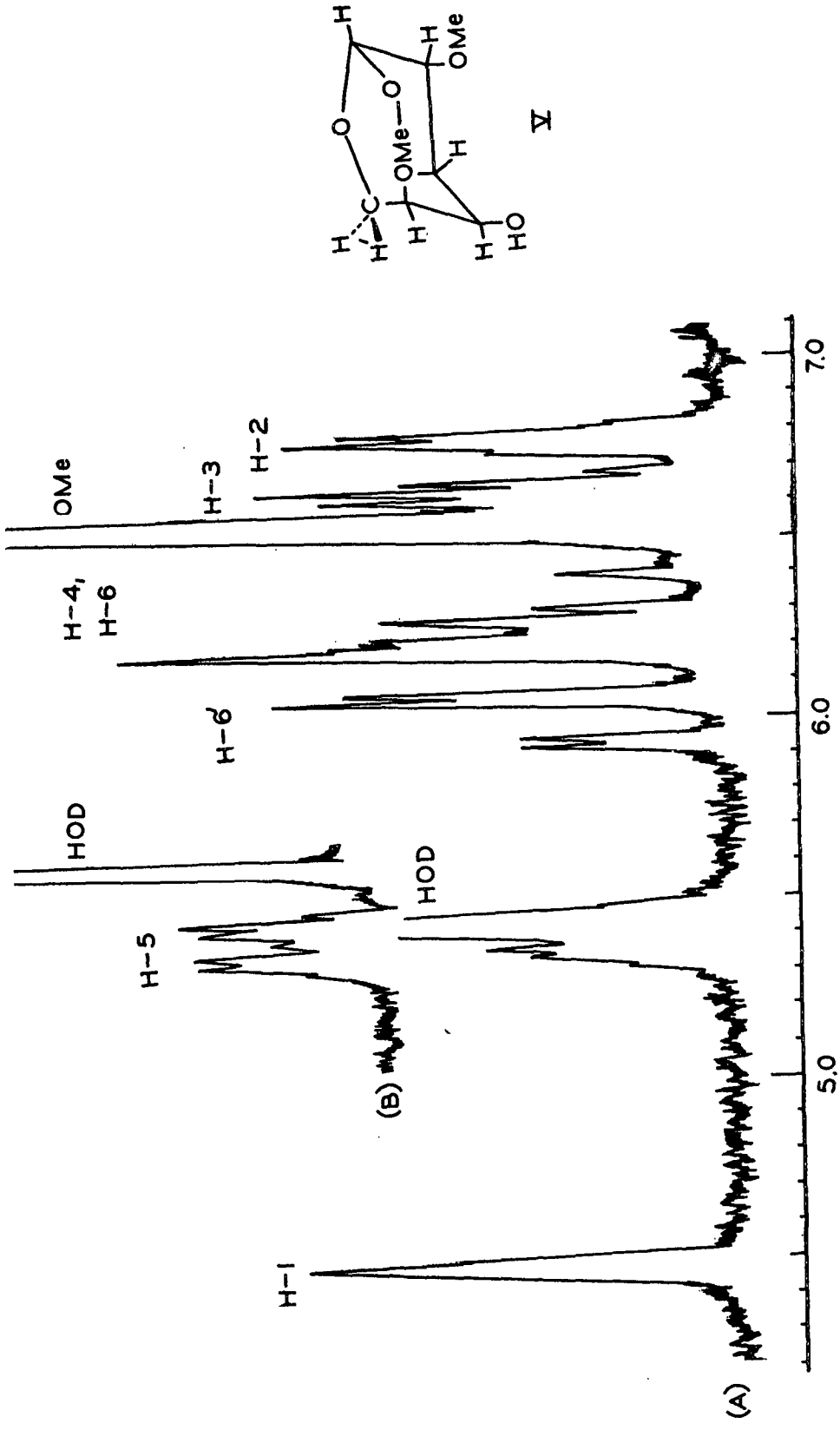


Figure 21. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-2,3-di-O-methyl-β-D-glucopyranose (V) in Deuterium Oxide, and (B) Partial Spectrum in Hot Deuterium Oxide

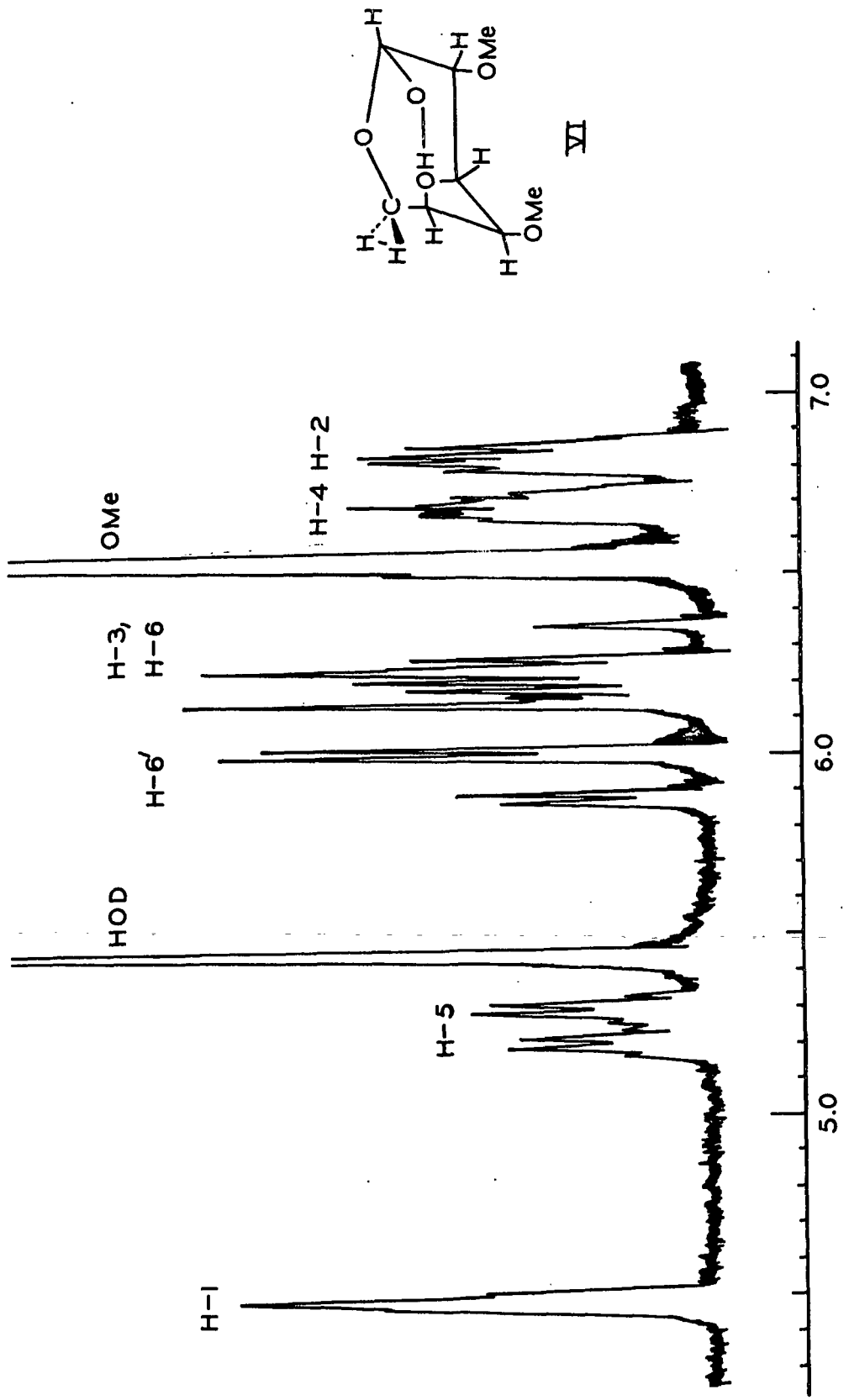
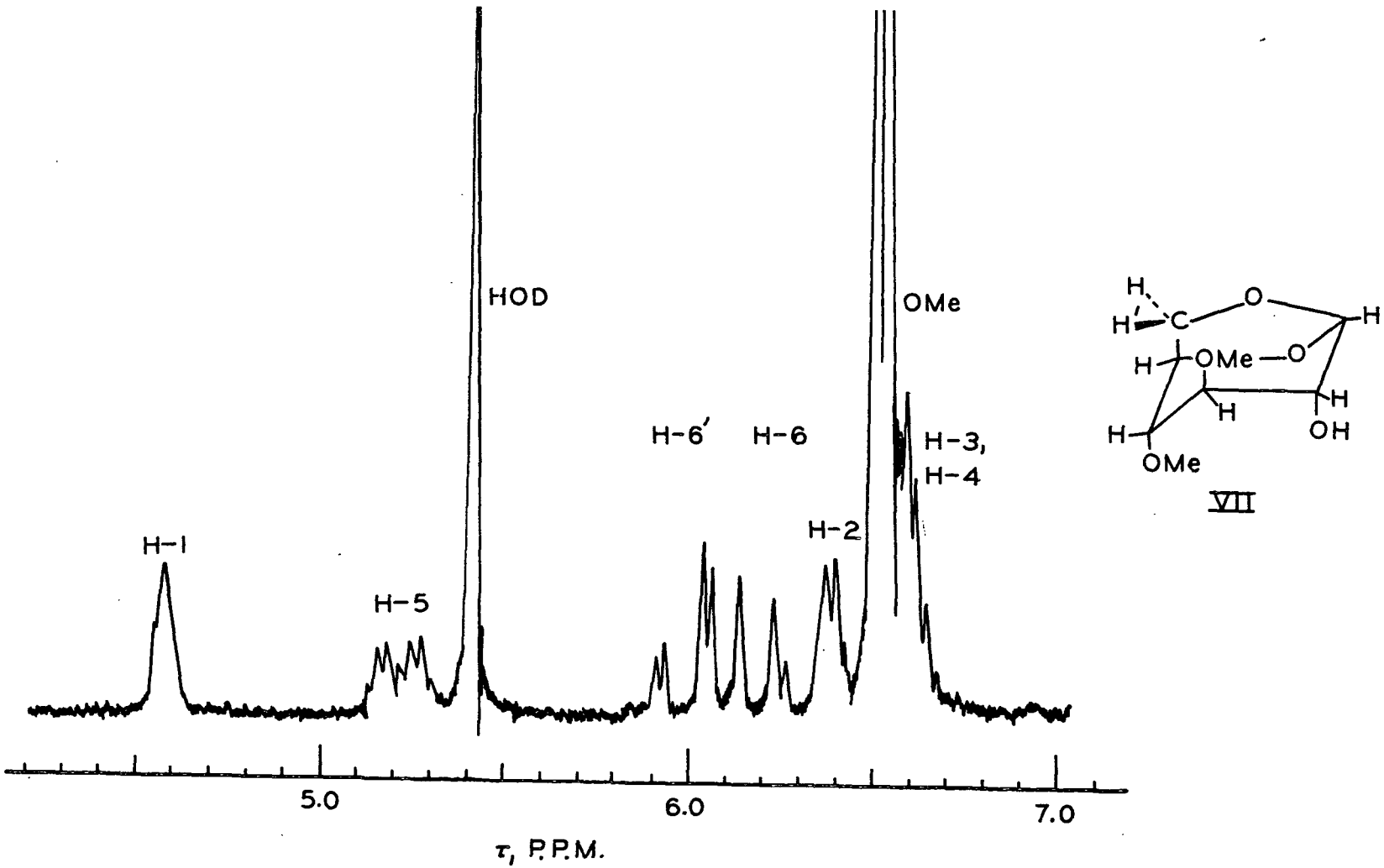


Figure 22. NMR Spectrum (60 MHz) of 1,6-Anhydro-2,4-di-O-methyl-β-D-glucopyranose (VI) in Deuterium Oxide



VII

Figure 23. NMR Spectrum (60 MHz) of 1,6-Anhydro-3,4-di-O-methyl-β-D-glucopyranose (VII) in Deuterium Oxide

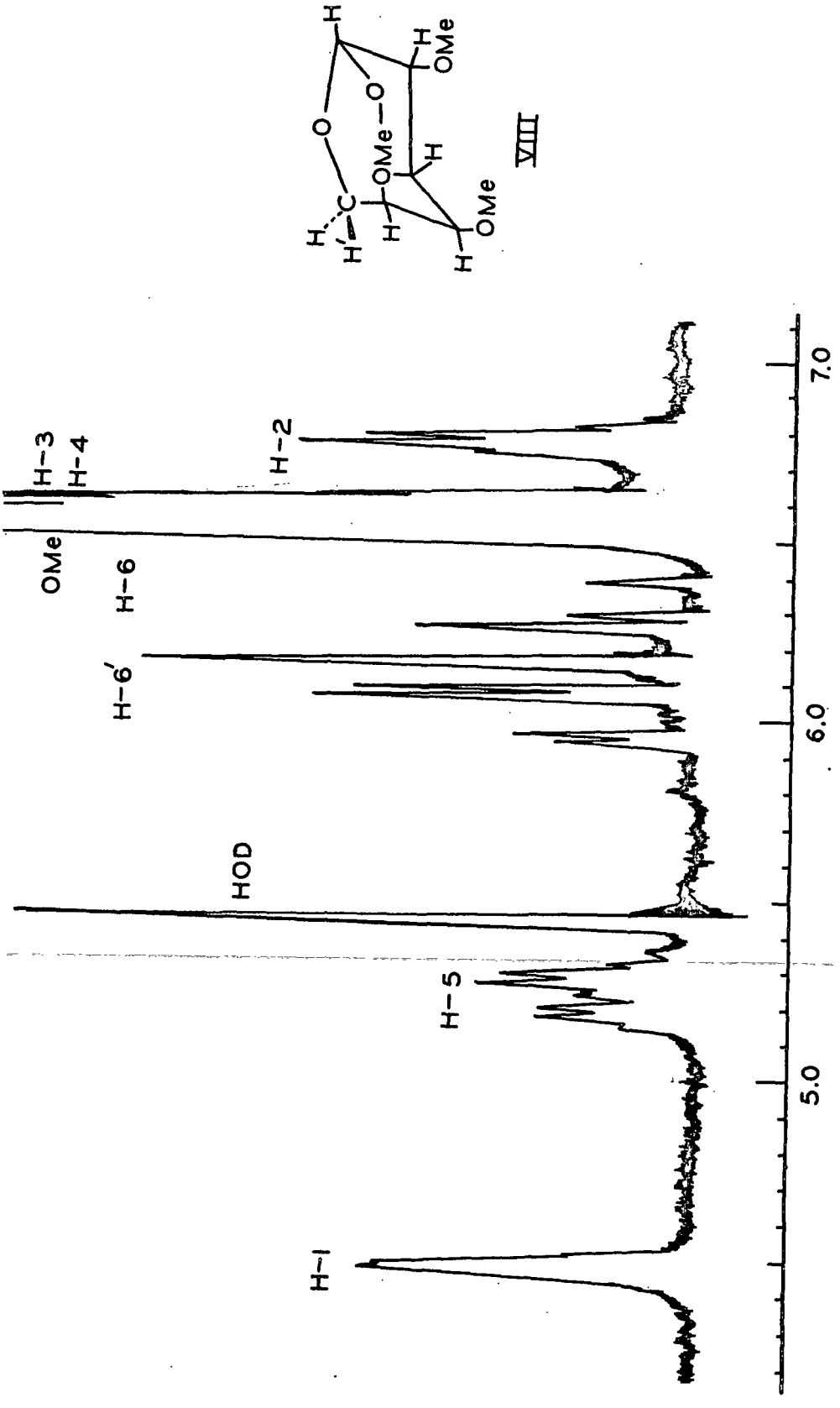
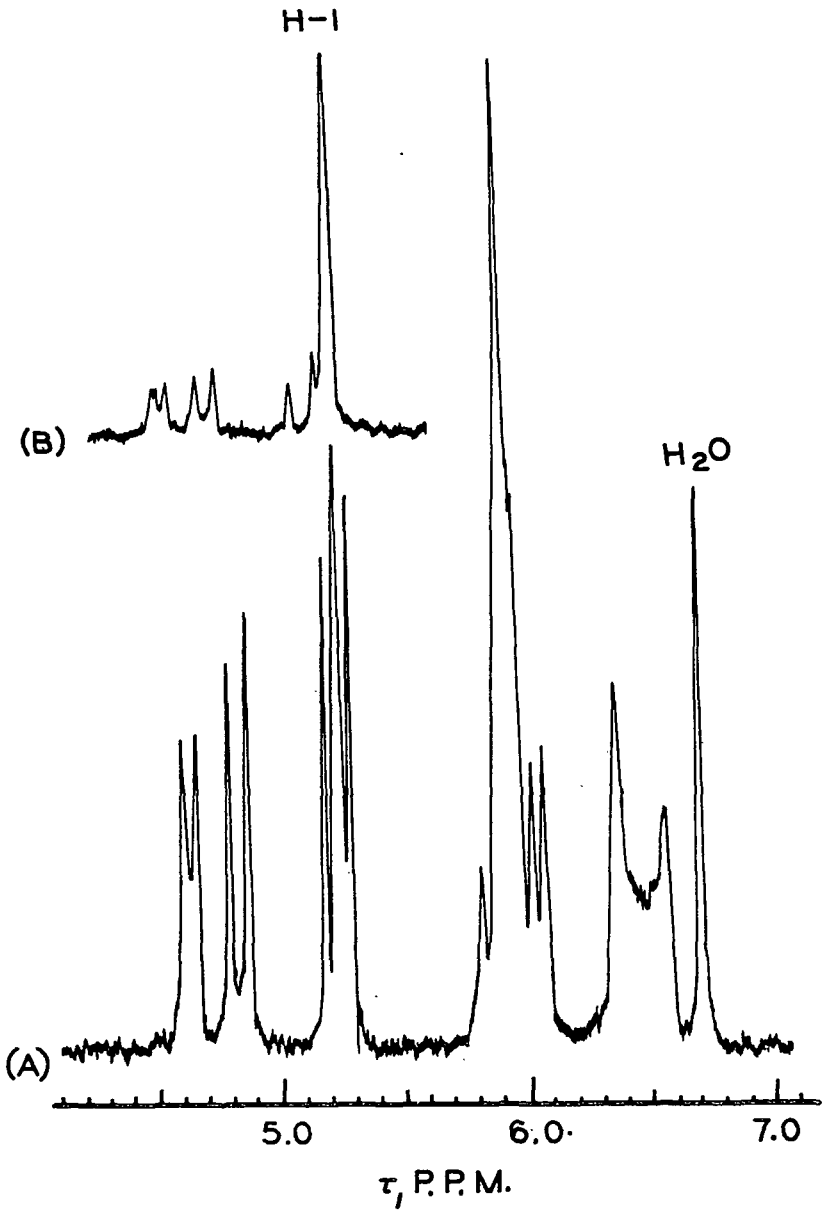


Figure 24. NMR Spectrum (60 MHz) of 1,6-Anhydro-2,3,4-tri-O-methyl-β-D-glucopyranose (VIII) in Deuterium Oxide



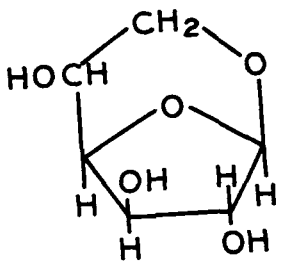
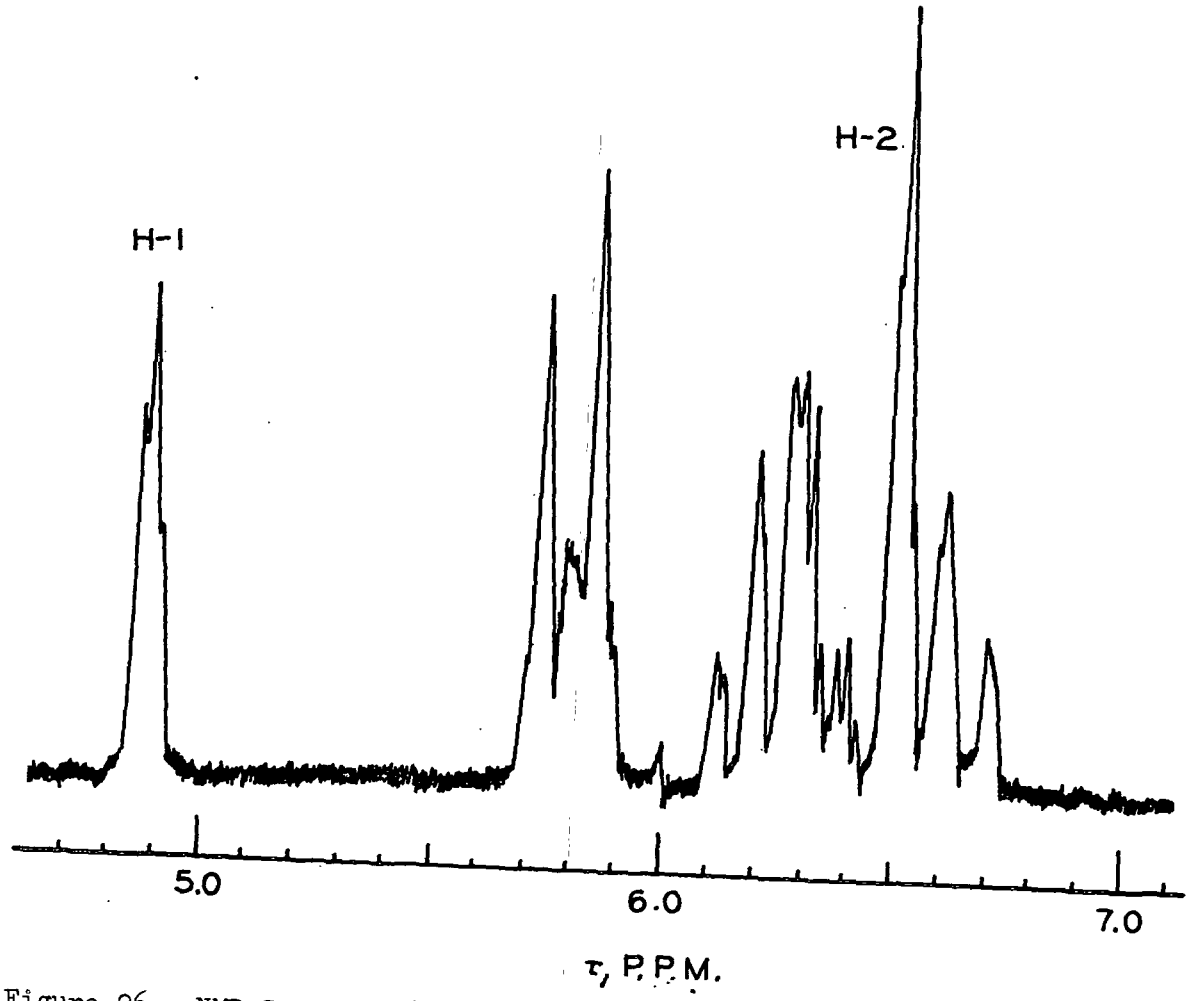
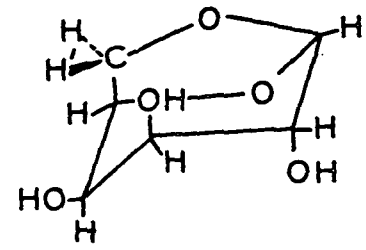


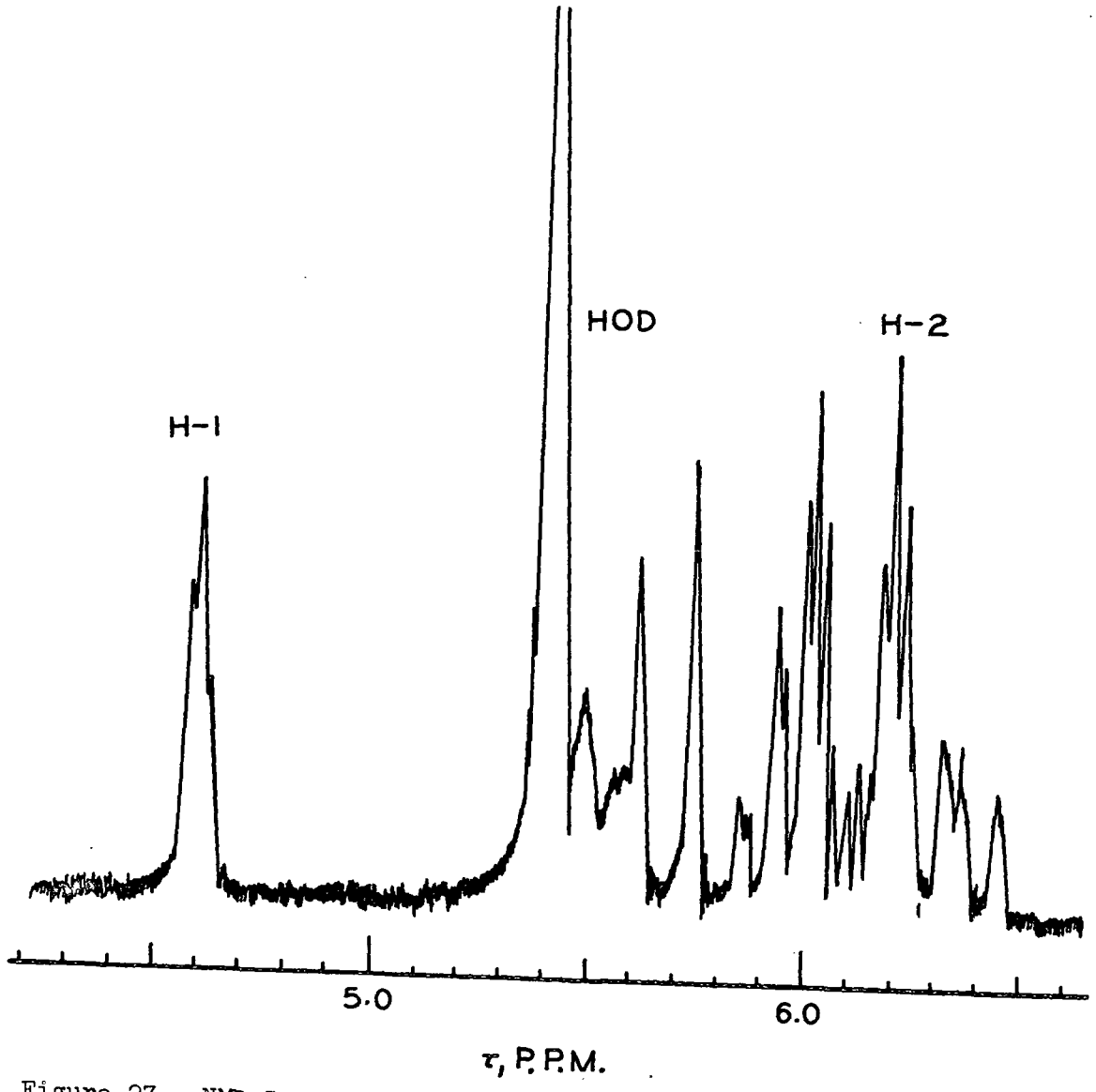
Figure 25. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-β-D-glucofuranose in Methyl Sulfoxide-$\underline{d}_6$, and (B) Partial Spectrum in Methyl Sulfoxide-$\underline{d}_6$ Containing Water

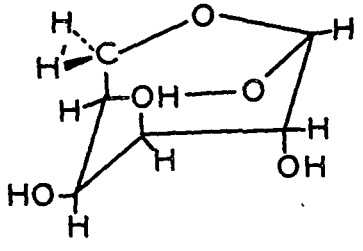




XII

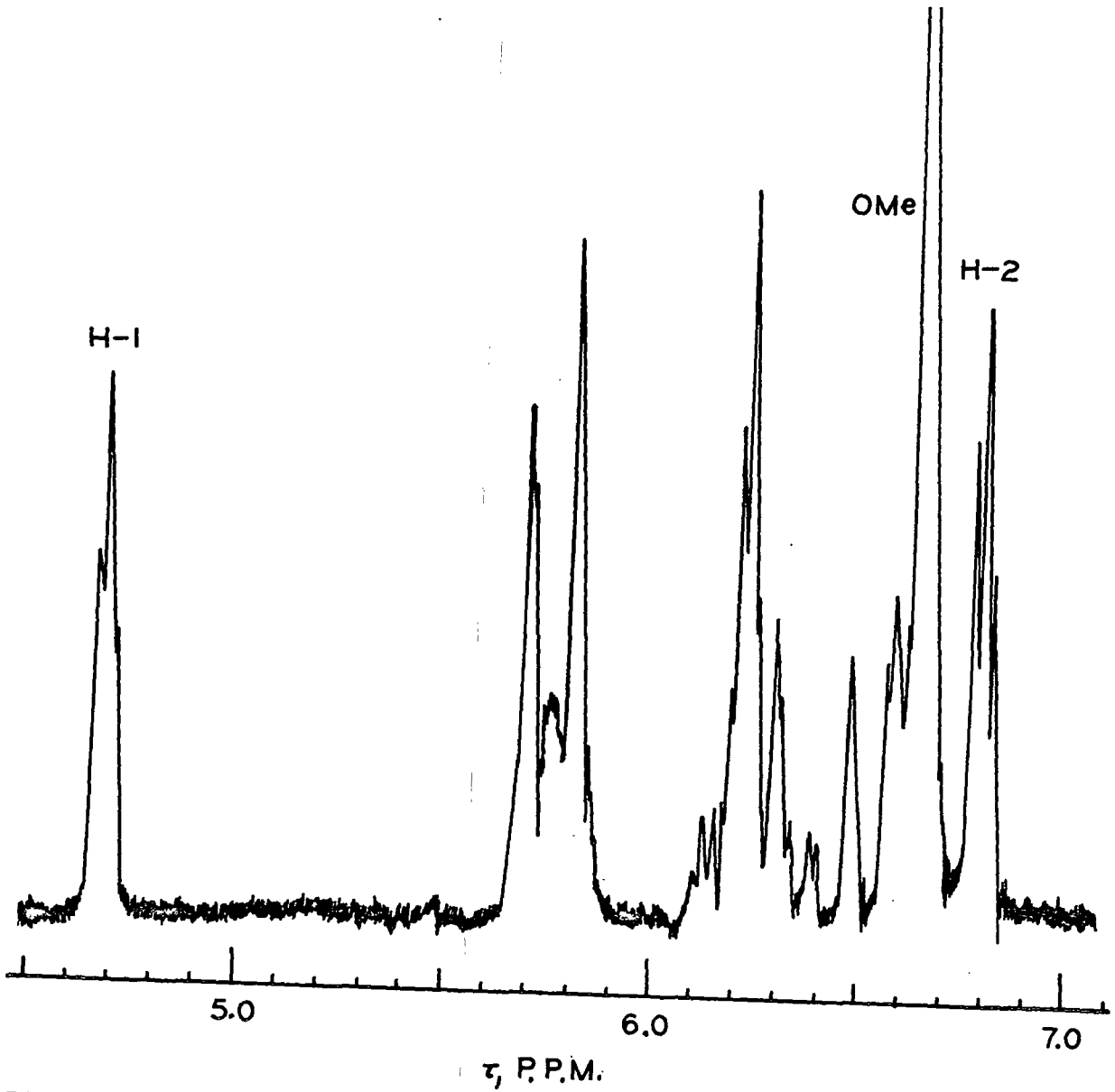
Figure 26. NMR Spectrum (60 MHz) of 1,6-Anhydro-β-D-galactopyranose (XII) in Methyl Sulfoxide-d_6 with Trace of Hydrogen Chloride Present

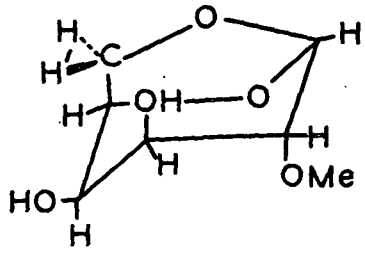




XII

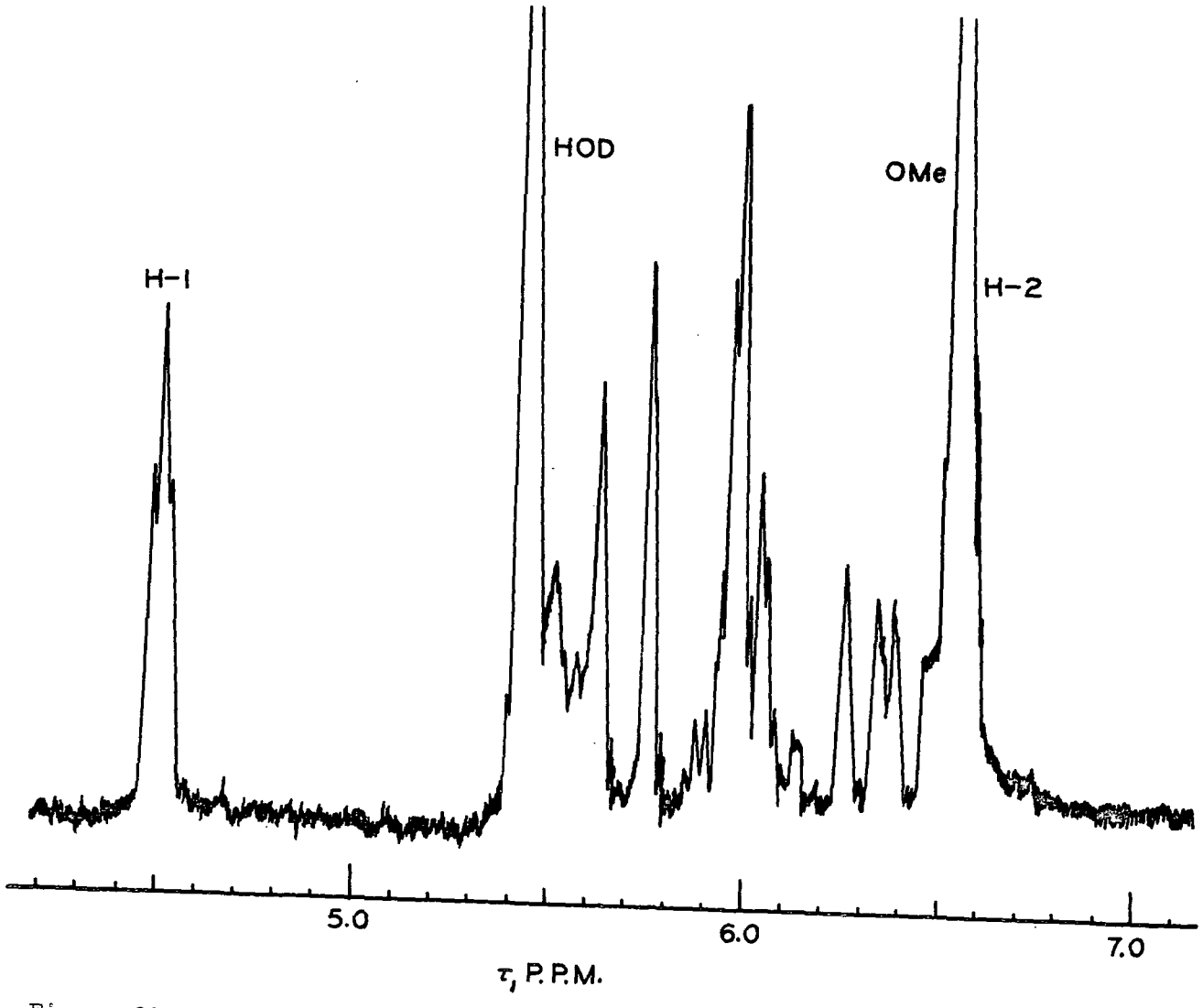
Figure 27. NMR Spectrum (60 MHz) of 1,6-Anhydro-β-D-galactopyranose (XII) in Deuterium Oxide

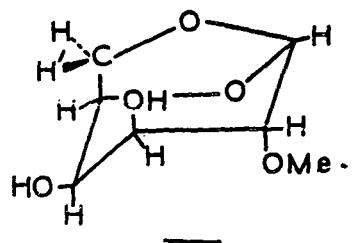




XIII

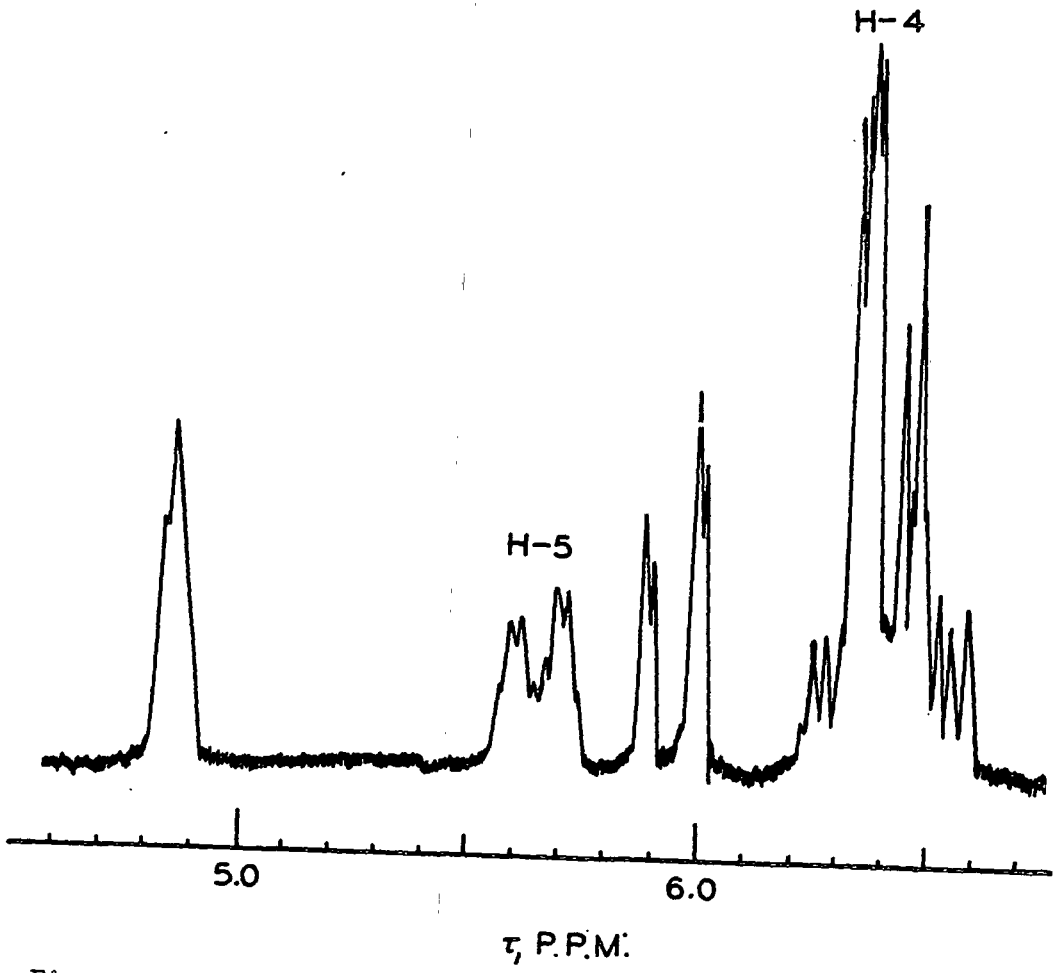
Figure 28. NMR Spectrum (60 MHz) of 1,6-Anhydro-2-O-methyl-β-D-galactopyranose (XIII) in Methyl Sulfoxide-d_6 with Trace of Hydrogen Chloride Present

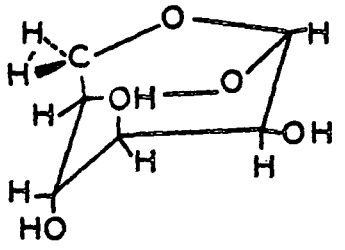




XIII

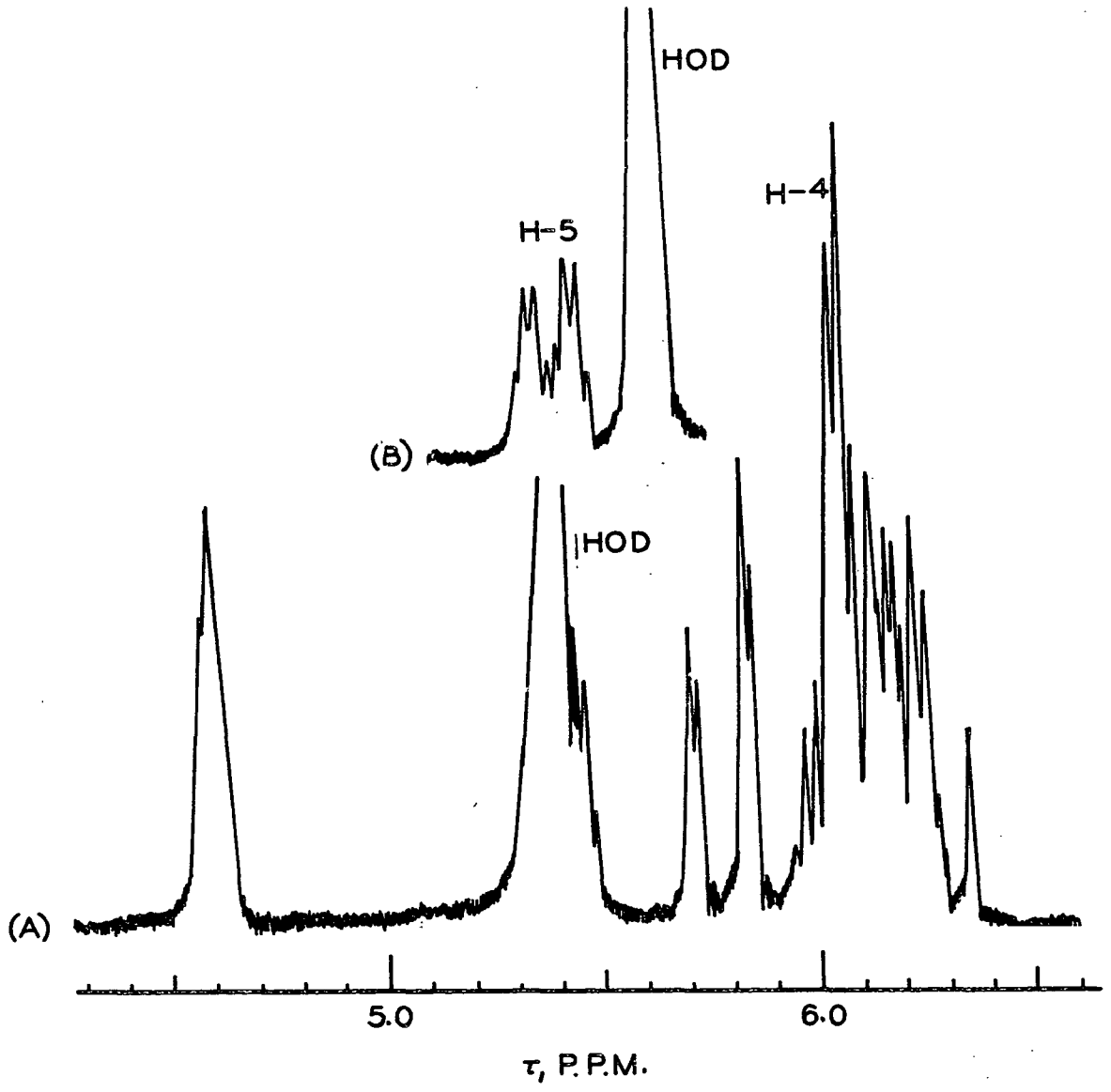
Figure 29. NMR Spectrum (60 MHz) of 1,6-Anhydro-2-O-methyl-β-D-galactopyranose (XIII) in Deuterium Oxide

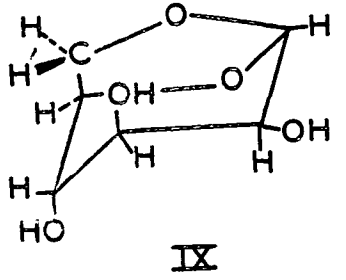




IX

Figure 30. NMR Spectrum (60 MHz) of 1,6-Anhydro-β-D-mannopyranose (IX) in Methyl Sulfoxide-$\underline{d}_6$ with Trace of Hydrogen Chloride Present





IX

Figure 31. (A) NMR Spectrum (60 MHz) of 1,6-Anhydro-β-D-mannopyranose (IX) in Deuterium Oxide, and (B) Partial Spectrum in Hot Deuterium Oxide

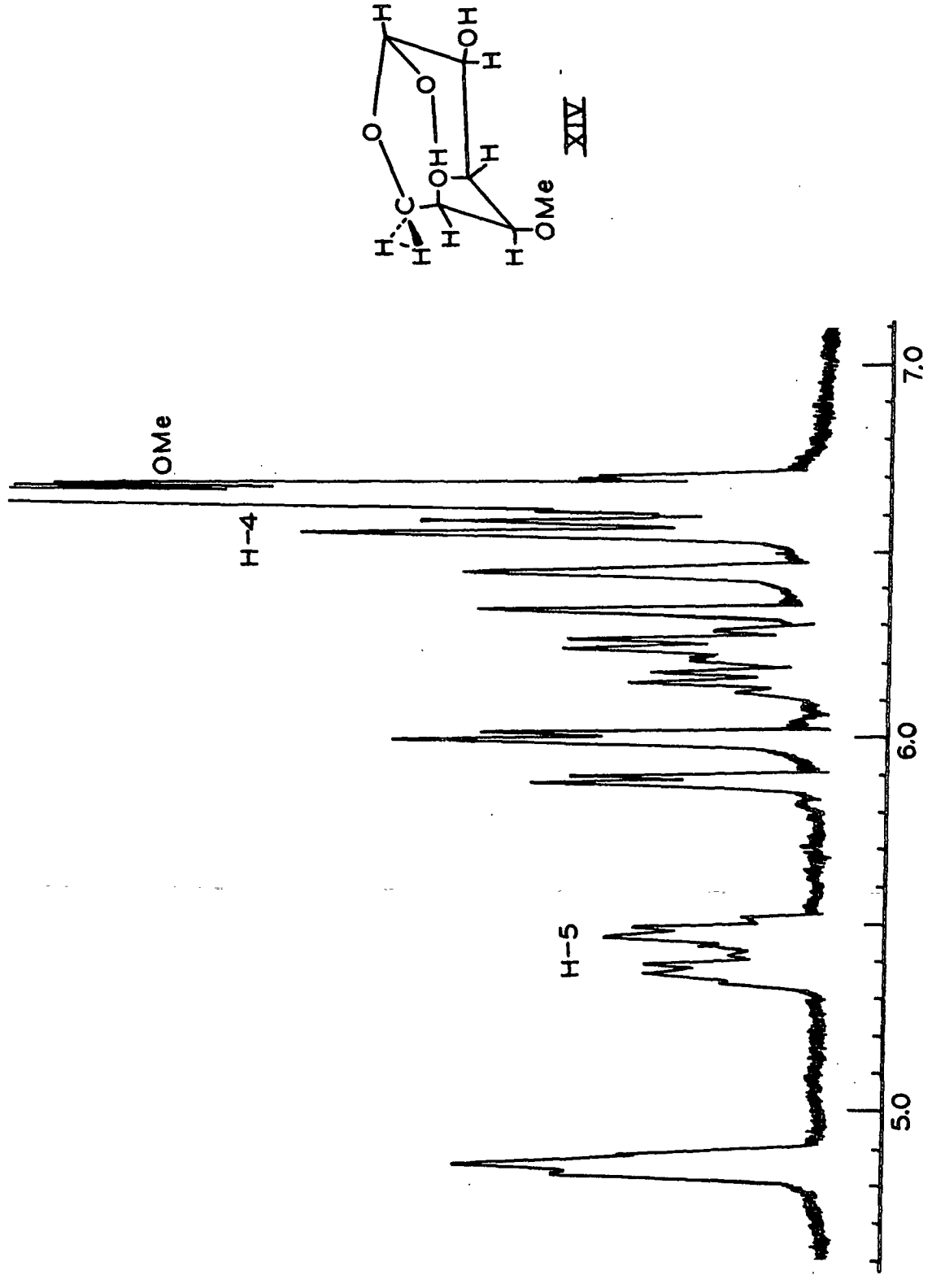
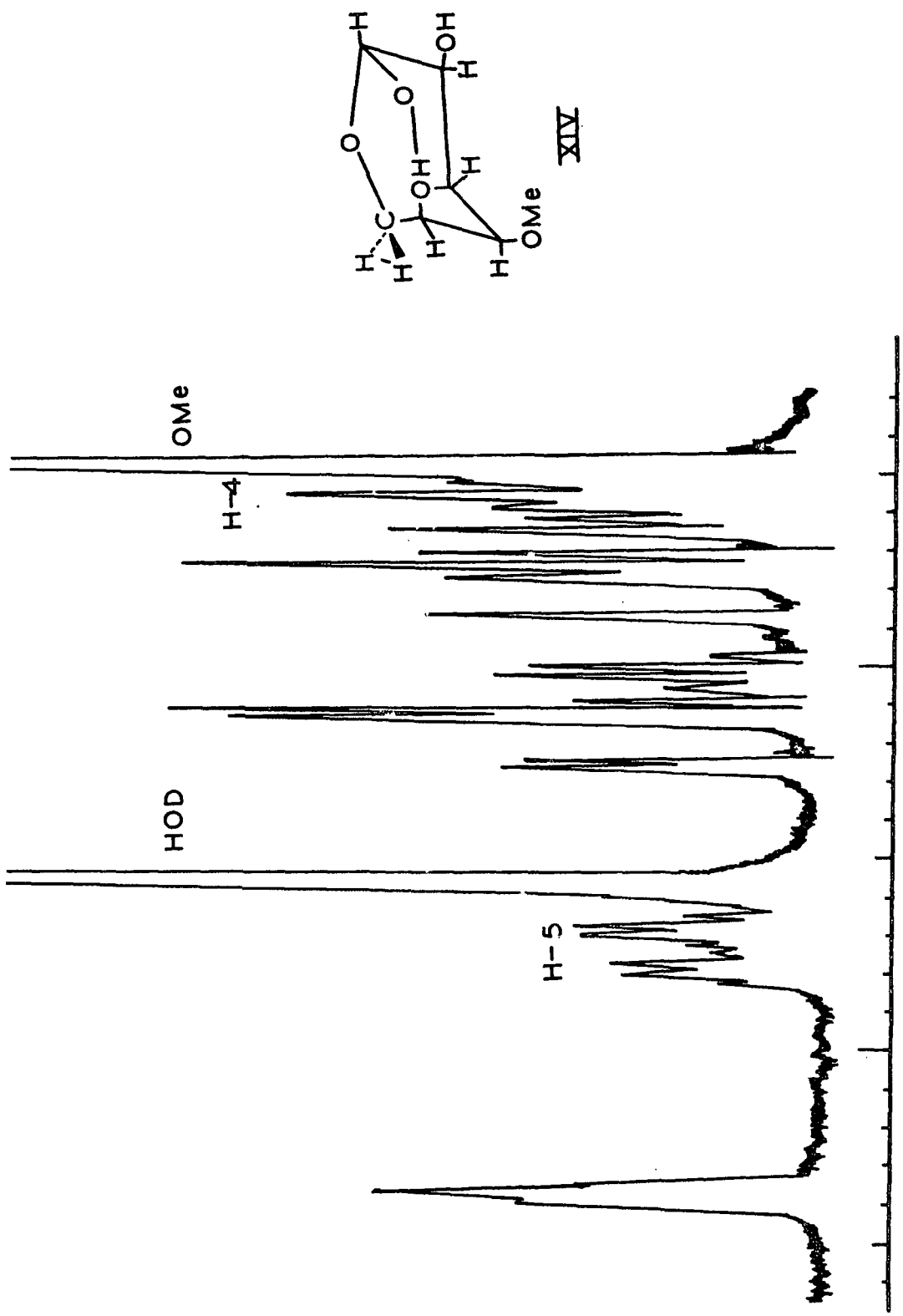


Figure 32. NMR Spectrum (60 MHz) of 1,6-Anhydro-4-O-methyl-β-D-mannopyranose (XIV) in Methyl Sulfoxide-d_6 with Trace of Hydrogen Chloride Present



XIV

Figure 33. NMR Spectrum (60 MHz) of 1,6-Anhydro-4-O-methyl-β-D-mannopyranose (XIV) in Deuterium Oxide

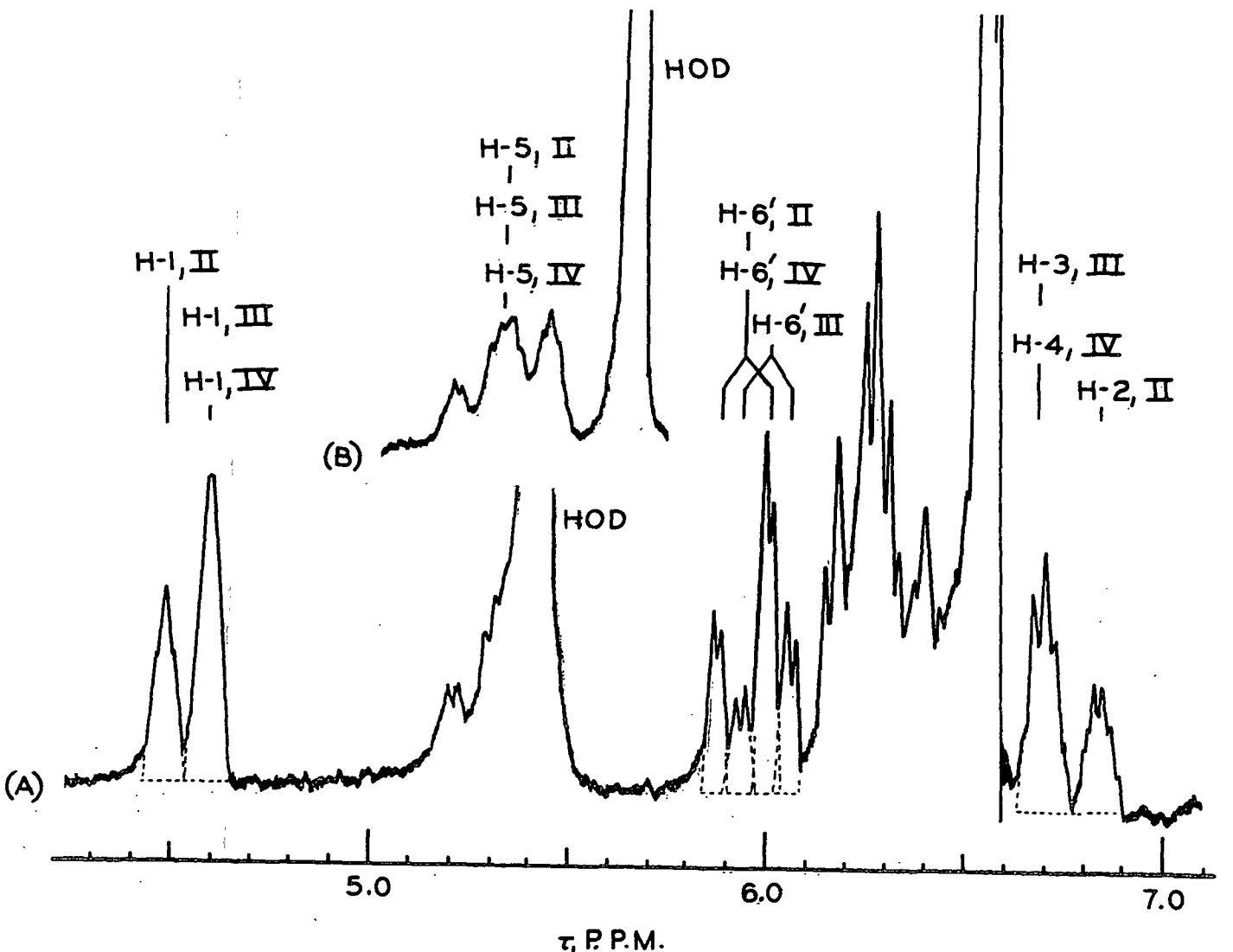


Figure 34. (A) NMR Spectrum (60 MHz) of a Mixture of Known Composition Containing 1,6-Anhydro-2-O-methyl-β-D-glucopyranose (II), 1,6-Anhydro-3-O-methyl-β-D-glucopyranose (III), and 1,6-Anhydro-4-O-methyl-β-D-glucopyranose (IV) in Deuterium Oxide, and (B) Partial Spectrum in Hot Deuterium Oxide

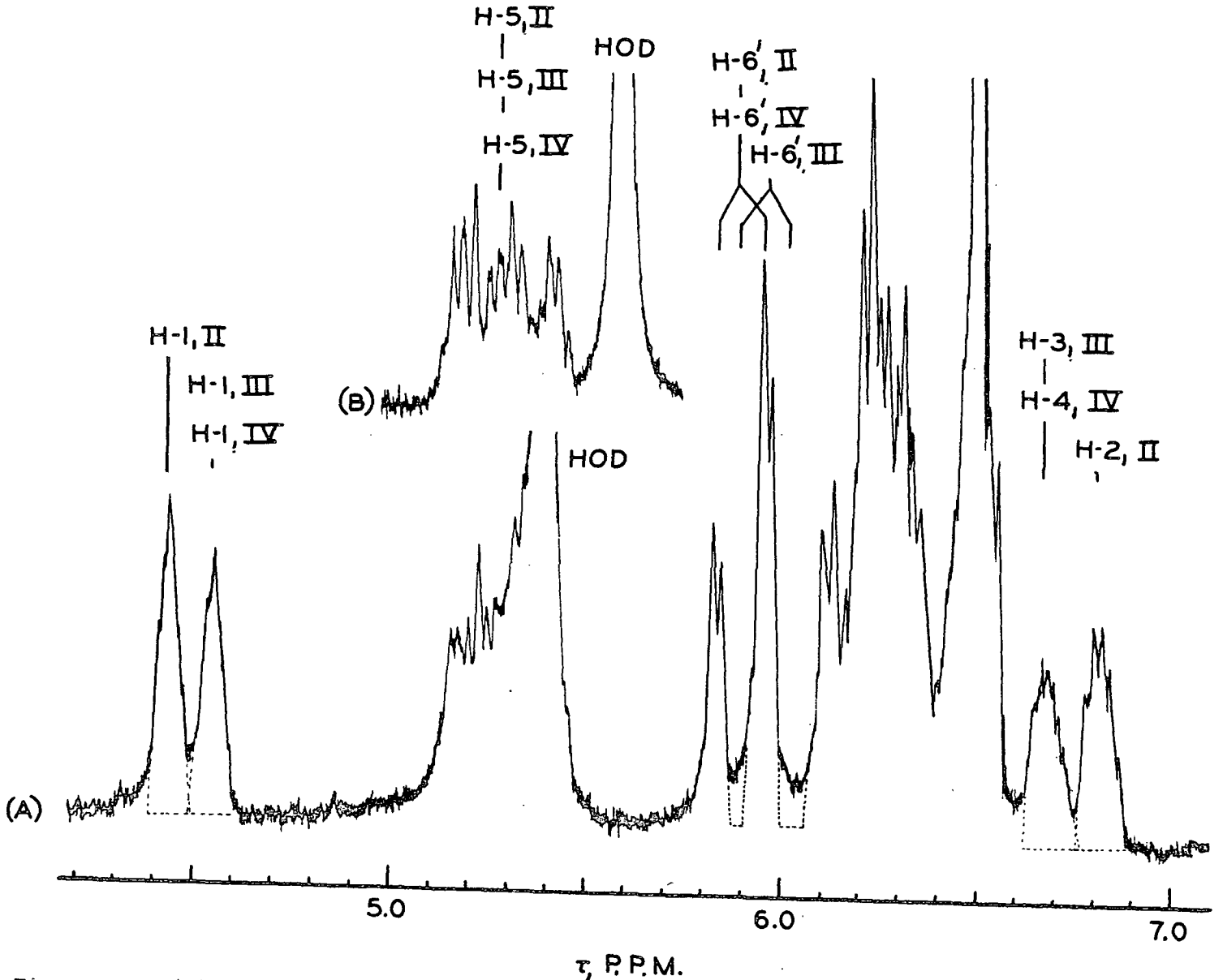


Figure 35. (A) NMR Spectrum (60 MHz) in Deuterium Oxide of Monomethyl Fraction Obtained by Reaction of 1,6-Anhydro-β-D-glucopyranose (I) with one Molar Equivalent Methyl Sulfate, and (B) Partial Spectrum in Hot Deuterium Oxide

APPENDIX IV

FIRST-ORDER COUPLING CONSTANTS FOR 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I) AND ITS METHYL ETHERS

TABLE XIII

FIRST-ORDER, COUPLING CONSTANTS FOR PROTON RESONANCES OF 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I) AND ITS METHYL ETHERS IN METHYL SULFOXIDE-$\underline{d}_6$ WITH TMS AS INTERNAL STANDARD

1,6-Anhydro-glucopyranose	Coupling Constant, $\underline{J}$, Hz									
	$\underline{J}_{1,2}$	$\underline{J}_{1,3}$	$\underline{J}_{2,3}$	$\underline{J}_{2,4}$	$\underline{J}_{3,4}$	$\underline{J}_{3,5}$	$\underline{J}_{4,5}$	$\underline{J}_{5,6'}$	$\underline{J}_{5,6}$	$\underline{J}_{6',6}$
Levoglucosan (I)	1.2	--	1.5	1.2	--	1.2	1.2	1.2	6.0	7.3
2-$\underline{O}$-Methyl-levoglucosan (II)	1.2	--	3.3	1.2	--	1.2	1.2	1.2	6.0	7.1
3-$\underline{O}$-Methyl-levoglucosan (III)	--	1.2	2.5	1.2	2.5	1.2	1.2	1.2	6.0	7.5
4-$\underline{O}$-Methyl-levoglucosan (IV)	1.2	--	3.5	1.2	3.0	1.2	1.2	1.2	6.0	7.5
2,3-Di-$\underline{O}$-methyl-levoglucosan (V)	1.2	1.2	3.3	1.2	3.0	1.2	1.5	1.5	6.0	7.5
2,4-Di-$\underline{O}$-methyl-levoglucosan (VI)	1.2	1.2	3.5	1.2	3.5	1.2	1.5	1.5	6.0	7.5
3,4-Di-$\underline{O}$-methyl-levoglucosan (VII)	1.2	1.2	--	1.2	--	1.2	1.5	1.5	6.0	7.5
Trimethyl-levoglucosan (VIII)	1.2	--	--	1.2	--	1.2	1.5	1.5	6.0	7.5

TABLE XIV

FIRST-ORDER, COUPLING CONSTANTS FOR PROTON RESONANCES OF 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I) AND ITS METHYL ETHERS IN DEUTERIUM OXIDE WITH DSS AS INTERNAL STANDARD

1,6-Anhydro-glucopyranose	Coupling Constant, J, Hz									
	$J_{1,2}$	$J_{1,3}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{5,6'}$	$J_{5,6}$	$J_{6',6}$
Levoglucosan (I)	1.2	--	2.0	1.2	--	1.2	1.5	1.2	6.0	7.5
2-O-Methyl-levoglucosan (II)	1.2	--	2.0	1.2	--	1.2	1.5	1.5	6.0	7.5
3-O-Methyl-levoglucosan (III)	--	1.2	3.0	--	3.0	1.2	1.5	1.5	6.0	7.5
4-O-Methyl-levoglucosan (IV)	--	--	--	1.2	3.0	1.2	1.5	1.5	6.0	7.5
2,3-Di-O-methyl-levoglucosan (V)	1.2	1.2	2.0	1.2	3.0	1.2	1.5	1.5	6.0	7.5
2,4-Di-O-methyl-levoglucosan (VI)	1.2	1.2	3.0	1.2	3.0	1.2	1.5	1.5	6.0	7.5
3,4-Di-O-methyl-levoglucosan (VII)	1.2	--	2.0	1.2	--	1.2	1.5	1.5	6.0	7.5
Trimethyl-levoglucosan (VIII)	1.2	--	2.0	1.2	--	1.2	1.5	1.5	6.0	7.5

APPENDIX V

POLYMERIZATION DATA FOR 1,6-ANHYDRO SUGARS

TABLE XV

POLYMERIZATION DATA[a] FOR 1,6-ANHYDRO-2-DEOXY-β-D-ARABINO-HEXOPYRANOSE (X)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.25	0.0027	0.0292	1.63	52	0.99
0.25	115	0.24	0.0023	0.0244	1.36	54	0.95
0.50	115	0.25	0.0023	0.0247	0.917	52	0.66
0.75	115	0.20	0.0021	0.0225	0.618	52	0.39
1	115	0.15	0.0016	0.0174	0.397	52	0.24

C_{IS} = 0.0628 g./ml.

C_{MCA} = 0.0139 g./ml.

[a]For definition of symbols in column headings see Experimental section on Polymerization of 1,6-anhydrides (p. 80).

TABLE XVI

POLYMERIZATION DATA FOR 1,6-ANHYDRO-β-D-MANNOPYRANOSE (IX)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	∿25	0.33	0.0019	0.0222	1.05	51	0.99
1.0	115	0.30	0.0018	0.0216	1.08	52	0.95
2.0	115	0.30	0.0021	0.0252	1.09	52	0.82
2.5	115	0.20	0.0024	0.0290	1.49	52	0.65
3.0	115	0.15	0.0023	0.0269	1.19	51	0.42
3.0	115	0.15	0.0022	0.0261	1.18	52	0.43
3.5	115	0.15	0.0019	0.0224	0.726	52	0.31
4.0	115	0.25	0.0019	0.0231	0.414	54	0.28
5.0	115	0.20	0.0023	0.0269	0.501	51	0.24
8.0	115	0.10	0.0019	0.0220	0.363	51	0.11

C_{IS} = 0.0628 g./ml.

C_{MCA} = 0.139 g./ml.

TABLE XVII

POLYMERIZATION DATA[a] FOR 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (I)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.30	0.0046	0.0441	1.07	52	0.99
0	~25	0.30	0.0042	0.0405	0.966	52	0.97
0.5	116	0.31	0.0049	0.0474	1.10	52	0.98
1.0	116	0.37	0.0062	0.0596	1.22	52	0.100
1.5	115	0.30	0.0054	0.0502	1.21	51	0.98
2.0	116	0.30	0.0052	0.0495	1.24	52	0.101
3.0	116	0.30	0.0049	0.0467	1.06	52	0.92
4.0	116	0.20	0.0041	0.0393	1.19	52	0.82
4.0	115	0.25	0.0048	0.0462	1.15	52	0.84
4.0[b]	115	0.25	0.0047	0.0450	1.08	52	0.82
6.0	115	0.20	0.0055	0.0526	0.879	52	0.45
6.0	115	0.20	0.0051	0.0491	0.813	52	0.45
6.0	115	0.30	0.0047	0.0456	0.510	54	0.45
9.0	115	0.070[c]	0.0030	0.0312[d]	0.540	54	0.17
12.0	115	0.060	0.0047	0.0455	0.442	52	0.08
18.0	115	0.30	0.0046	0.0444	0.240	52	0.02
24.0	115	0.25	0.0	0.0298	0.943	∞	0.99

[a] C_{IS} = 0.130 g./ml.; C_{MCA} = 0.112 g./ml.
[b] 0.005 ml. benzene present.
[c] C_{IS} = 0.137 g./ml.
[d] C_{MCA} = 0.123 g./ml.

TABLE XVIII

POLYMERIZATION DATA[a] FOR 1,6-ANHYDRO-β-D-GALACTOPYRANOSE (XII)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.10	0.0016	0.0169	1.54	52	0.98
3.0	115	0.20	0.0024	0.0252	1.10	52	0.94
5.0	115	0.19	0.0021	0.0224	1.05	54	0.95
7.0	115	0.19	0.0023	0.0245	1.08	54	0.90
8.0	115	0.20[b]	0.0026	0.0271	0.627	51	0.64
10.0	115	0.20[b]	0.0026	0.0279	0.546	54	0.42

[a] C_{IS} = 0.102 g./ml.

C_{MCA} = 0.123 g./ml.

[b] C_{IS} = 0.132 g./ml.

TABLE XIX

POLYMERIZATION DATA FOR 1,6-ANHYDRO-4-O-(β-D-GLUCOPYRANOSYL)-β-D-GLUCOPYRANOSE (XI)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.30	0.0024	0.0129	1.24	52	0.99
2.0	116	0.50	0.0042	0.0227	1.26	52	0.95
6.0	116	0.40	0.0048	0.0258	1.58	52	0.84
8.0	116	0.39	0.0044	0.0236	1.23	52	0.70
12.0	116	0.60	0.0042	0.0223	0.568	52	0.52
17.0	116	0.42	0.0036	0.0194	0.490	52	0.36

C_{IS} = 0.0279 g./ml.

C_{MCA} = 0.0311 g./ml.

TABLE XX

POLYMERIZATION DATA FOR 1,6-ANHYDRO-4-O-METHYL-β-D-GLUCOPYRANOSE (IV)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.21	0.0020	0.0225	0.570	51	1.02
4.0	115	0.20	0.0019	0.0220	0.463	54	0.81
8.0	115	0.21	0.0020	0.0228	0.361	52	0.64
14.0	115	0.10	0.0027	0.0308	0.727	52	0.45
23.0	115	0.15	0.0019	0.0218	0.233	52	0.31

C_{IS} = 0.137 g./ml.

C_{MCA} = 0.123 g./ml.

TABLE XXI

POLYMERIZATION DATA FOR 1,6-ANHYDRO-3-O-METHYL-β-D-GLUCOPYRANOSE (III)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.15	0.0018	0.0184	0.717	51	1.01
4.0	115	0.20	0.0023	0.0236	0.626	51	0.91
9.0	115	0.20	0.0026	0.0272	0.657	52	0.83
24.0	115	0.10	0.0018	0.0184	0.630	51	0.59
48.0	115	0.040	0.0018	0.0181	1.21	52	0.46

C_{IS} = 0.130 g./ml.

C_{MCA} = 0.112 g./ml.

TABLE XXII

POLYMERIZATION DATA[a] FOR 1,6-ANHYDRO-2-O-METHYL-β-D-GALACTOPYRANOSE (XIII)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.22	0.0018	0.0207	0.486	52	1.00
4.0	116	0.20	0.0017	0.0197	0.459	52	0.90
16.0	116	0.20[b]	0.0023	0.0258	0.499	51	0.71
34.0	115	0.12[b]	0.0024	0.0271	0.668	51	0.54
39.0	115	0.25	0.0023	0.0259	0.251	51	0.47
60.0	115	0.10	0.0021	0.0237	0.456	51	0.37

[a] C_{IS} = 0.145 g./ml.

C_{MCA} = 0.123 g./ml.

[b] C_{IS} = 0.138 g./ml.

TABLE XXIII

POLYMERIZATION DATA FOR 1,6-ANHYDRO-3,4-DI-O-METHYL-β-D-GLUCOPYRANOSE (VII)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.20	0.0018	0.0224	0.554	52	0.99
12.0	115	0.20	0.0019	0.0234	0.503	52	0.86
35.0	115	0.15	0.0021	0.0263	0.572	54	0.65
48.0	114	0.15	0.0020	0.0247	0.457	52	0.56
61.0	114	0.11	0.0022	0.0276	0.598	52	0.48

C_{IS} = 0.138 g./ml.

C_{MCA} = 0.123 g./ml.

TABLE XXIV

POLYMERIZATION DATA[a] FOR 1,6-ANHYDRO-2-O-METHYL-β-D-GLUCOPYRANOSE (II)

Polymerization Time, hr.	Polymerization Temp., °C.	V_{IS}, ml.	V_{MCA}, ml.	W_{Mo}, g.	$\langle A_M/A_{IS} \rangle$	Mole Ratio, Mo/MCA	F_M
0	~25	0.20[b]	0.0024[c]	0.0252	0.701	52	0.99
4	115	0.15	0.0017	0.0199	0.663	54	0.94
9	115	0.10	0.0018	0.0201	1.01	51	0.95
17	116	0.10[d]	0.0018	0.0203	0.875	51	0.86
23	115	0.16	0.0021	0.0240	0.641	52	0.81
52	115	0.10	0.0021	0.0240	0.812	52	0.64

[a] C_{IS} = 0.138 g./ml.
C_{MCA} = 0.123 g./ml.

[b] C_{IS} = 0.130 g./ml.

[c] C_{MCA} = 0.112 g./ml.

[d] C_{IS} = 0.145 g./ml.